J. Fetal Med. (June 2015) 2:83–86
DOI 10.1007/s40556-015-0047-x

BRIEF COMMUNICATION

Antenatal Diagnosis of Klippel–Trenaunay–Weber Syndrome

Ashutosh Gupta[1] · **Anjila Aneja**[2] · **Sanjay Mehta**[3] · **Pankaj Saini**[3]

Received: 20 March 2015 / Accepted: 21 July 2015 / Published online: 6 August 2015

Abstract Klippel–Trenaunay–Weber syndrome (KTWS) is a rare congenital disease characterized by cutaneous hemangiomas, soft tissue, and bone hypertrophy. It may be associated with arteriovenous malformation involving deeper pelvic organs. We present a prenatally-diagnosed case of KTWS identified at 26 weeks. Antenatal ultrasound identified subcutaneous hemangioma with soft tissue hypertrophy with unilateral hypertrophy of the lower extremity with right renal hydronephrosis. During the rest antenatal period, KTWS did not deteriorate and was not complicated by acute enlargement and sequestration and Kasabach–Merritt syndrome.

Keywords Hemangioma · Hypertrophy · Sequestration

Introduction

Klippel–Trenaunay–Weber syndrome (KTWS) is a rare cutaneous vascular disorder characterized by triad of subcutaneous hemangioma (port-wine stain), malformation of capillary, venous, or lymphatic vessels presenting as varicose veins and soft tissue or bony hypertrophy. It may involve deeper veins with arteriovenous fistula involving pelvic organs and/or vagina [1]. This syndrome was first described by Klippel and Trenaunay in 1900 [2] but the prenatal diagnosis by ultrasound was documented only in 1981 by Hatjis et al. [3].

Majority of the cases have all the three components of the triad but hemangioma is the most common feature with most affected organ being the leg [4]. Hemangiomas (port-wine stain) are mostly apparent at birth, and mostly are capillary in nature [5]. Venous damage is due to weakness in the smooth muscle along with defective valves. Bone and soft tissue hypertrophy is due to abnormal angiogenesis.

Report of Case

A primigravida with 26 weeks of gestation was referred for evaluation of right renal hydronephrosis. On ultrasound examination, the fetus was identified to have cutaenous hemangioma and soft-tissue hypertrophy involving the right buttock, anterolateral aspect of the right thigh, right-sided hydronephrosis, right patent processus vaginalis, and right inguinal hernia (Figs. 1, 2). Ultrasound examination revealed a complex lesion involving the subcutaneous region of the right buttock, anterolateral aspect of right thigh with internal septa. The lesion had low pressure vascularity with marked soft-tissue hypertrophy. There was no evidence of omphalocele, macrosomia, macroglossia, macrodactyly and any osseous bony lesion. Her personal and family history was unremarkable. The length of the femur, tibia, and fibula in both the limbs appeared normal and matching, that is, at 26 weeks, there was no obvious bone length discrepancy. But during follow-up scans, the right femur was identified to be growing at a faster rate as compared to the left side, which was confirmed in the postnatal examination of the fetus (Fig. 3).

✉ Ashutosh Gupta
dr_ashutosh75@rediffmail.com

[1] Department of Fetal Medicine and Clinical Geneticist, Max Super Speciality Hospital, West Block, 1 Press Enclave Road, Saket, New Delhi 110017, India

[2] Department of Minimal Access & OBGYN, Fortis Memorial Research Institute, Gurgaon, Haryana, India

[3] Department of Radiology, Artemis Health Institute, Gurgaon, Haryana, India

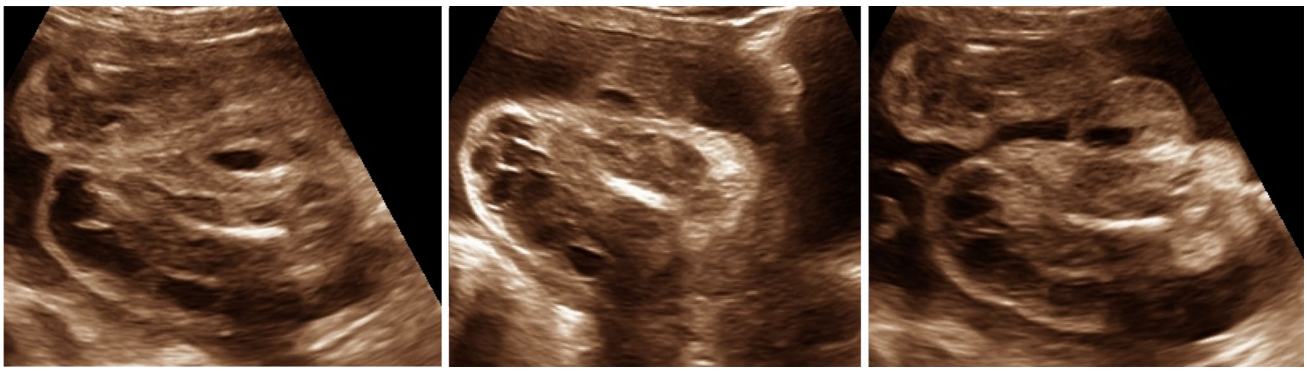

Fig. 1 Multiple subcutaneous hemangioma and soft-tissue hypertrophy on the anterolateral aspect of the right thigh and involving right buttock

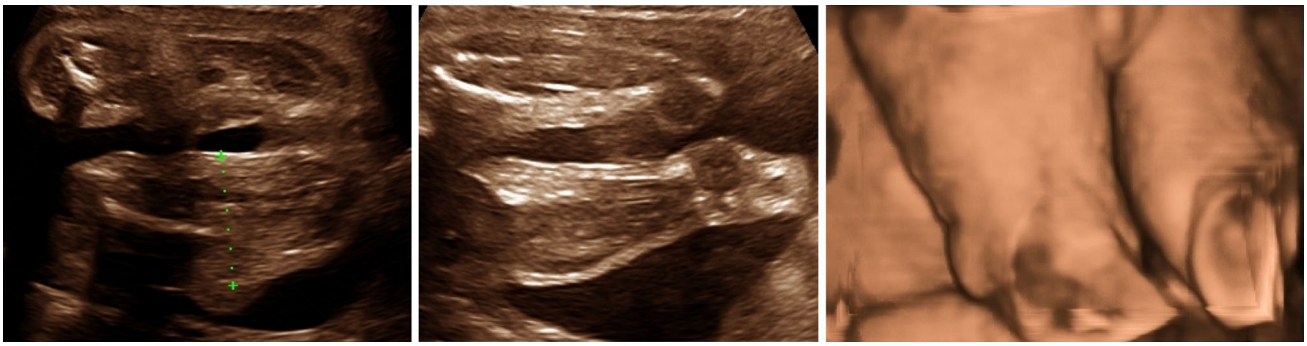

Fig. 2 Antenatal ultrasound depicting the limb asymmetry in the circumference involving both, thigh and calf, which is delineating sharply in 4D scan

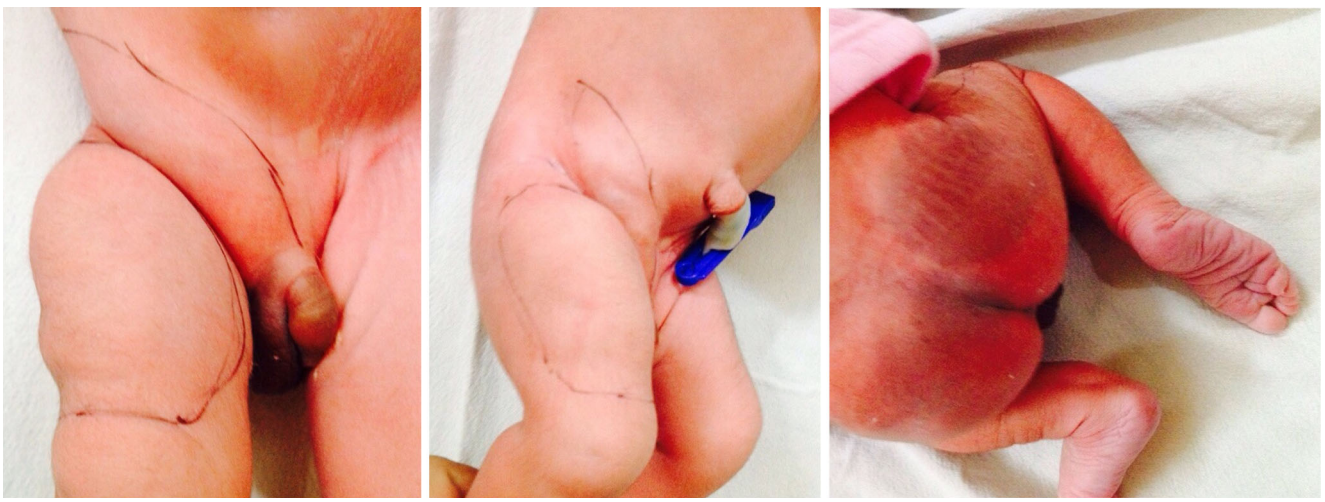

Fig. 3 Postnatal examination of the baby shows subcutaneous swelling (soft tissue hypertrophy) over the anterolateral aspect of the thigh with port-wine stain over the buttocks with right inguinal hernia

The fetus was followed up weekly for further increase in the lesion or appearance of new or retroperitoneal hemangioma with signs of hydrops, cardiomegaly with high output cardiac failure, or polyhydramnios. The parents were counseled regarding the potential of its enlargement, acutely leading to sequestration and acute anemia which is known as Kasabach–Merrit syndrome and fetal hydrops due to acute anemia. Multiple subcutaneous lesions were suggestive of hemangiomatous lesion. Amniotic fluid and placental thickening remained within normal limits. Peak

systolic velocity in middle cerebral artery was also appropriate for the 50th centile for the gestational age. The baby was delivered vaginally and the prenatal findings were confirmed on postnatal examination. The right buttock and lower extremity had multiple subcutaneous hemangioma with port-wine discoloration with right-limb hypertrophy. Complete blood count of the newborn baby were within normal limits.

The varicose veins can be managed by surgical interventions like venous ligation,vein stripping, resection, and amputation. However, as the deep venous system is atretic, success of the surgical endeavor is not guaranteed and the surgical decision has to be individualized. Other safer surgical options are also available like endovenous thermal ablation or sclerotherapy. Nonsurgical management like compression garments may be used to manage the chronic venous insufficiency, lymphedema, recurrent cellulitis, and bleeding. Prenatal discrepancy in the blood supply and angiopoietin leads to limb hypertrophy and lengthening leading to vertebral scoliosis and gait abnormality, requiring surgical correction and physiotherapy. Infants with KTWS should have annual checkups supplemented with medical or surgical intervention, if required, so as to avoid any complications due to hemangioma.

Discussion

Recent theory suggests KTWS to be a mixed meso- and ectodermal abnormality, primarily, due to defective angiogenesis [6]. The syndrome has been hypothesized to be due to prenatal imbalance in production and regulation of angiopoietin-2 [7], with alteration in vascular remodelling [8]. It has been found to be associated with balanced chromosomal translocation between (5;11)(q13.3;p15.1) [9] and (8;14)(q22.3;q13) [10].

KTWS may be complicated with nonimmune hydrops fetalis, polyhydramnios, high output cardiac failure, and consumptive coagulopathy due to hemangioma-associated diffuse intravascular coagulation.

Close differentials of KTWS are:

Proteus syndrome (overgrowth of skin, bones, muscles, fatty tissue, blood and lymphatic vessels; skin overgrowth, atypical bone development, partial or regional gigantism, macrodactyly with tumor predisposition); **Beckwith–Wiedemann syndrome** (an overgrowth disorder usually present at birth characterized by combination of exomphalos, macroglossia, and gigantism); **lymphangioma** (malformations of the lymphatic system, mainly involving head and neck, most of which, are benign, soft and slow growing); and **Maffucci syndrome** (a sporadic disease characterized by multiple enchondromas which are symmetrical in distribution, benign enlargement of cartilage, enchondromas, bone deformities, and hemangiomas). KTWS may have a life-threatening complication like bleeding in internal organs such as gastrointestinal tract, genitourinary system, spleen, liver, and central nervous system. Large vascular lesions may lead to sequestration of platelets and consumptive coagulopathy known as Kasabach–Merritt syndrome. It is characterized by thrombocytopenia, coagulation defects, and complications arising due to them [11].

Conclusion

KTWS is a rare mixed meso- and ectodermal abnormality due to defective angiogenesis. Weakness in smooth muscle with defective venous valves leads to varicose veins. Imbalance in angiopoietin levels prenatally, with abnormal angiogenesis leads to soft tissue and bony hypertrophy. Usually the course is benign but might be associated with life-threatening complication, e.g., bleeding in internal organs like gastrointestinal tract, genitourinary system, spleen, liver, and central nervous system. Large vascular lesions may lead to sequestration of platelets and consumptive coagulopathy known as Kasabach–Merritt syndrome which might lead to thrombocytopenia, coagulation defects, and complications arising due to them.

The lesion after being identified confidently on antenatal ultrasound, warranted close fetal surveillance for any further increase or new appearance of lesions for recognition and prevention of complications for future. Close monitoring of the fetus was required to observe high output cardiac failure, nonimmune hydrops fetalis, and cardiomegaly and prompt delivery to manage the fetus in intensive neonatal care.

Compliance with Ethical Standards

Conflict of Interest None

Ethical statement The manuscript has not been submitted any other for simultaneous consideration. The manuscript has not been published previously (partly or in full). A single study is not split up into several parts. No data have been fabricated or manipulated (including images) to support our conclusions. No data, text, or theories by others are presented as if they were the author's own ("plagiarism"). Co-authors have adequately contributed to the work.

Informed consent Informed consent was obtained from all individual participants included in the study. This is a retrospective study—"For this type of study, formal consent is not required".

References

1. Fait G, Daniel Y, Kupferminc MJ, et al. Klippel-Trenaunay-Weber syndrome associated with fetal growth restriction. Hum Reprod. 1996;11:2544–5.

2. Klippel M, Trenaunay P. Du naevus vanquex osteohypertrophique. Arch Gin Med. 1990;3:641–72.
3. Hatjis CG, Philip AG, Anderson GG, et al. The in utero ultrasonographic appearance of Klippel–Trenaunay–Weber syndrome. Am J Obstet Gynecol. 1981;139(8):972–4.
4. Meine JG, Schwartz RA, Janniger CK. Klippel–Trenaunay–Weber syndrome. Cutis. 1997;60(3):127–32.
5. Samuel M, Spitz L. Klippel-Trenaunay syndrome: clinical features, complications and management in children. Br J Surg. 1995;82(6):757–61.
6. Baskervill PA, Ackroyd JS, Browse NL. The etiology of the Klippel-Trenaunay syndrome. Ann Surg. 1985;202(5):624–7.
7. Hu Y, Li L, Seidelmann SB, et al. Identification of association of common AGGF1 variants with susceptibility for Klippel-Trenaunay syndrome using the structure association program. Ann Hum Genet. 2008;72(5):636–43.
8. Berry SA, Peterson C, Mize W, et al. Klippel-Trenaunay syndrome. Am J Med Genet. 1998;79(4):319–26.
9. Whelan AJ, Watson MS, Porter FD, et al. Klippel-Trenaunay-Weber syndrome associated with a balanced translocation. Am J Med Genet. 1995;59(4):492–4.
10. Wang Q, Timur AA, Szafranski P, et al. Identification and molecular characterization of de novo translocation t (8;14)(q22.3;q13) associated with a vascular and tissue overgrowth syndrome. Cytogenet Cell Genet. 2001;95(3–4):183–8.
11. Zoppi MA, Ibba RM, Floris M, et al. Prenatal sonographic diagnosis of Klippel-Trénaunay-Weber syndrome with cardiac failure. J Clin Ultrasound. 2001;29(7):422–6.