Magnetic Resonance Angiography in Clubfoot and Vertical Talus

A Feasibility Study

Lisa Kruse BS, Christina A. Gurnett MD, PhD,
David Hootnick MD, Matthew B. Dobbs MD

Published online: 6 January 2009
© The Association of Bone and Joint Surgeons 2008

Abstract Congenital vascular alterations of the normal adult arterial pattern have been associated with multiple congenital limb deformities including clubfoot and vertical talus. Investigators have observed absence of the anterior tibial artery and dorsalis pedis artery in most patients with clubfoot, and absence of the posterior tibial artery in all patients with vertical talus. We used magnetic resonance angiography to define the lower extremity vascular anatomy of two patients with left-sided vertical talus and right-sided clubfoot and one patient with bilateral vertical talus and cartilage-derived morphogenetic protein-1 (CDMP-1) gene mutation. Of the three patients, one had bilateral

posterior tibial artery deficiencies while the other had bilateral anterior tibial artery deficiencies. The third patient with bilateral vertical talus and CDMP-1 mutation had normal arterial structure bilaterally. Though clubfoot and vertical talus have distinctly different clinical phenotypes, the association of each with arterial abnormalities suggests a common etiology during development. The presence of normal arterial structure in our patient with vertical talus and CDMP-1 mutation suggests that other nonvascular etiologies may be responsible for some cases of foot deformities.

Level of Evidence: Level IV, prognostic case series. See the Guidelines for Authors for a complete description of levels of evidence.

The authors are supported by NIH NINDS K12 Award (NS01690), the Children's Discovery Institute, and March of Dimes Basil O'Connor Award (CAG); and by the Shriners Hospital for Children, the Saint Louis Children's Hospital Foundation, and the Pediatric Orthopaedic Society of North America (MBD).

Each author certifies that his or her institution has approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

L. Kruse, C. A. Gurnett, M. B. Dobbs (✉)
Department of Orthopedic Surgery, Washington University
School of Medicine, One Children's Place, Suite 4S60, St. Louis,
MO 63110, USA
e-mail: dobbsm@wudosis.wustl.edu

C. A. Gurnett
Department of Neurology, Washington University School
of Medicine, St. Louis, MO, USA

D. Hootnick
Department of Orthopedic Surgery, State University
of New York Health Science Center, Syracuse, NY, USA

M. B. Dobbs
St. Louis Shriners Hospital for Children, St. Louis, MO, USA

Introduction

The normal adult arterial blood supply to the ankle and foot is generally provided by three arteries: posterior tibial, anterior tibial, and peroneal. However, alteration of this normal arterial pattern has been documented to occur at a much higher frequency in patients with either clubfoot or vertical talus than in the general population [2, 4, 8, 9, 16, 20, 25, 26]. Such consistent observations regarding arterial alteration combined with the fact that rapid skeletal and embryonic arterial development occur around the fifth week of embryonic life suggest the skeletal and arterial abnormalities may have a common origin [13].

Based on cadaveric dissections, the frequency of absent or substantially smaller arteries in the lower leg in normal adult limbs ranges from 2.4% (4/165) to 7.1% (88/1239) for the anterior tibial artery and 4.9% (24/486) to 8.4% (32/380) for the posterior tibial artery [21]. Arteriography in the lower limbs of clubfoot patients prior to surgery has

revealed anterior tibial artery absence or deficiency in 89% (63/71) of limbs [25]. Two separate studies demonstrated that in feet with vertical talus subjected to arteriography, all (7/7 [26] and 1/1 [2]) of the limbs had an absent or greatly reduced posterior tibial artery. Another study reported a variety of lower extremity limb defects associated with either an absence or severe deficiency of the anterior tibial artery and the dorsalis pedis including congenital fibular deficiency, congenital tibial aplasia with polydactyly, congenital tibial aplasia with talocalcaneal synostosis [17].

Most of the data gathered thus far regarding the prevalence of vascular anomalies with lower limb bone abnormalities has been performed using conventional arteriography [2, 4, 9, 12, 15, 25, 26], a procedure that is accurate but also invasive with risks including arterial damage, hemorrhage, ischemia, and reduction in limb growth.

Doppler ultrasound is an alternative noninvasive technique to study the arterial pattern. It is, however, less accurate than arteriography. In one study of patients with lower limb anomalies and known arteriographically demonstrated deficiencies, arterial patterns detected by Doppler ultrasound were interpreted as normal in 32% (9/28) of limbs [25]. One limitation of Doppler ultrasound is its inability to simultaneously determine vessel size and depth, resulting in difficulties detecting subtle vascular anomalies such as primitive preserved vessels.

Magnetic resonance angiography is a minimally invasive technique that has been used to image vascular structures in the abdomen, pelvis, and lower extremities for a variety of clinical indications [22]. The images produced are equivalent to angiographic images, and the technique does not carry the risks of radiation or an arterial puncture [22].

The purpose of this study was to illustrate the technique of magnetic resonance arteriography in visualizing the arterial structures of the lower limbs in pediatric patients with clubfoot and vertical talus deformities. We also describe the vascular abnormalities that were present in one patient with a known genetic etiology of congenital vertical talus.

Materials and Methods

Three pediatric patients with congenital foot abnormalities from St. Louis Shriners Hospital for Children were examined by magnetic resonance angiography scans to map their lower extremity arterial system. A single board-certified radiologist (TH) interpreted the studies, giving special attention to the origination, termination, and caliber of the anterior tibial artery, posterior tibial artery, peroneal artery, dorsalis pedis, and plantar arches. None of the patients had arteriography.

Magnetic resonance (MR) exams were performed on a 1.5 T scanner (Siemens Medical Systems, Islin, NH) using the body coil. Bright blood MR images were obtained using a 3-D spoiled gradient-echo pulse sequence in the coronal plane after a manual injection of gadolinium contrast agent administered intravenously through a peripheral catheter. This sequence provides high-resolution images with near isotropic voxels and minimizes pulsatility artifacts. For every patient, dynamic scans were acquired from the pelvis to the foot in the arterial phase of the contrast agent passage without any superimposition of venous structures. The images were transferred to a dedicated workstation for 3-D reconstruction.

Case Reports

Patient 1

Patient 1 was a male newborn of Caucasian descent who presented with a right-sided clubfoot and left-sided vertical talus deformity. The patient was born at 36 weeks gestation and delivered by cesarean section. The pregnancy was complicated by maternal diabetes requiring insulin. Orthopaedic evaluation and treatment of the vertical talus and clubfoot deformities began at 6 weeks of age. Treatment of the clubfoot deformity was with the Ponseti method [18] and treatment of the vertical talus deformity was with a new technique that minimizes the need for extensive surgery [1, 6, 7].

Magnetic resonance arteriography of bilateral lower extremities was performed when patient was 22 months of age. This revealed bilateral abnormalities of the posterior tibial artery (Fig. 1). On the vertical talus (left) side, the posterior tibial artery was only 1 mm in diameter and became even smaller as it crossed the ankle. The anterior tibial artery was the dominant artery on the left side at 2.3 mm at its greatest diameter and fed the dorsalis pedis artery. The peroneal artery on the left was only 1 mm in diameter; it trifurcated and then terminated above the ankle. The clubfoot (right) side had an absent posterior tibial artery at the level of the peroneal artery trunk. The anterior tibial artery (1.5 mm diameter) and peroneal artery (1.6 mm diameter) were codominant.

Patient 2

Patient 2 was a male newborn of Caucasian descent who presented with a right-sided clubfoot and left-sided vertical talus deformity as well as sacral agenesis. The patient was delivered vaginally at 38 weeks of gestation with no complications. Before presentation to our clinic at the age

Fig. 1 Magnetic resonance angiography of the lower extremities in Patient 1 with right-sided clubfoot and left-sided vertical talus deformities. A complete absence of the posterior tibial artery is noted on the right and a diminished posterior tibial artery on the left. (Narrow straight arrow = posterior tibial artery; wide straight arrow = anterior tibial artery; large triangular arrow head = peroneal artery).

of 3 months, the patient had undergone four sets of long-leg plaster casts changed weekly in attempt to correct his foot deformities. Treatment was initiated at the time of presentation to our clinic using the Ponseti method [18] for the clubfoot deformity and a recently described method for vertical talus that involves serial casting and minimal surgery [1, 6, 7].

Magnetic resonance arteriography of bilateral lower extremities was performed when the patient was 18 months of age and revealed bilateral anterior tibial artery deficiency (Fig. 2). The vertical talus (left) side had an absent anterior tibial artery with a normal-appearing posterior tibial artery and peroneal artery. The clubfoot (right) side had an anterior

Fig. 2 Magnetic resonance angiography of the lower extremities of Patient 2 with right-sided clubfoot and left-sided vertical talus deformities. A complete absence of the anterior tibial artery is noted on the left and a diminished anterior tibial artery on the right. (Narrow straight arrow = posterior tibial artery; wide straight arrow = anterior tibial artery; large triangular arrow = peroneal artery).

tibial artery that terminated just below the knee and a peroneal artery that was diminished in size. The right posterior tibial artery was present and of normal caliber.

Patient 3

Patient 3 was a female newborn of Caucasian descent who presented with bilateral vertical talus. The patient was delivered vaginally at 37 weeks of gestation with no complications. Family history was significant for a brother, paternal grandmother, and paternal great grandmother with bilateral vertical talus. In addition, there was a first cousin with bilateral calcaneovalgus foot deformities as well as multiple relatives with congenital hand abnormalities including brachydactyly and clinodactyly. We previously reported a mutation in the CDMP-1 (cartilage-derived morphogenetic protein-1) gene believed responsible for the limb anomalies seen in this family [5]. The patient presented to our orthopaedic clinic at the age of 5 months at which time treatment was initiated. The vertical talus deformities were treated with serial casting followed by extensive soft tissue releases.

Fig. 3 Magnetic resonance angiography showing Patient 3, who had a genetic mutation in *CDMP-1* which has a known association with familial vertical talus. Patient 3 had bilateral vertical talus deformity. This is a posterior view showing normal vascular structure with an anomalous branch of the popliteal artery on the left. (Wide arrow = anterior tibial artery; narrow arrow = posterior tibial artery; dotted arrow = peroneal artery).

Magnetic resonance angiography of bilateral lower extremities was performed when the patient was 6 years of age and demonstrated the presence of the anterior tibial artery, the posterior tibial artery, and the peroneal artery bilaterally (Fig. 3). Arteries were of normal caliber and all contributed the arterial flow in the ankle and foot.

Discussion

We chose to study two rare individuals with co-occurring vertical talus and clubfoot, in order to better understand the vascular etiology of these conditions. The two patients with co-occurring vertical talus and clubfoot had the same vessel absent or diminished in both their clubfoot and vertical talus sides, though the two patients were missing different vessels. Patient 1 had deficient posterior tibial arteries and Patient 2 had deficient anterior tibial arteries. The presence of both lower limb abnormalities in a single patient, combined with the magnetic resonance angiography findings, raises the possibility that clubfoot and vertical talus are different phenotypic expressions of the same

Table 1. Magnetic resonance angiography results and their relation to phenotypic deformity

Patient/limb	Deformity	ATA	PTA	Peroneal
1 / right	TEV	Normal	Absent	Giant
2 / right	TEV	Absent	Normal	Small
1 / left	CVT	Normal	Small	Small
2 / left	CVT	Small	Normal	Normal
3 / right	CVT	Normal	Normal	Normal
3 / left	CVT	Normal	Normal	Normal

TEV = talipes equinovarus/clubfoot; CVT = congenital vertical talus; ATA = anterior tibial artery; PTA = posterior tibial artery.

etiological process (Table 1). To give better insight on whether vertical talus and clubfoot indeed share a common origin, however, it will be important to perform magnetic resonance angiography on a larger group of vertical talus and clubfoot patients. Previous research demonstrated a strong correlation between an absent anterior tibial artery in clubfoot and an absent posterior tibial artery in vertical talus [2, 4, 9, 12, 15, 25, 26]. This correlation did not hold true in the current study. Vertical talus was seen to occur in one case with an anterior tibial artery deficiency and in another case with a posterior tibial artery deficiency. The same observation was seen for clubfoot with deficiency in either of these arteries documented. It is likely, therefore, that the reduction in the number of vessels supplying the limb produces the risk of developing clubfoot or vertical talus, rather than the absence of any particular artery.

Vascular disruptions are believed associated with a variety of musculoskeletal birth defects ranging from isolated limb anomalies such as transverse limb deficiency to multisystem disorders such as Goldenhar syndrome [14, 19]. This syndrome consists of a variable constellation of birth defects involving underdevelopment of bones (middle ear ossicles, mandible, zygomatic arch, malar bone) and muscles (mastication and facial expression) in the head similar to variable involvement of underdeveloped bones (talus, fibula, femur, tibia) and muscles (gastrocnemius) in congenital lower extremity malformations. Animal models of Goldenhar syndrome variations in phenotype related to the location, duration, and severity of a hematoma formation during development, resulting in hypoxia and developmental arrest [19]. The similarity of arterial anomalies in various congenital limb deformities (clubfoot, vertical talus, fibular deficiency, proximal femoral focal deficiency) suggests that these anomalies arise from a single teratogenic event, such as a localized hemorrhage and hypoxia or an abnormality in normal development (ie, apoptosis), before the seventh week of fetal development.

Congenital vascular deficiencies in the lower extremities may occur in unaffected control individuals [21]

suggesting that the presence of a vascular deficiency alone is not sufficient to cause limb deformities. However, we hypothesize that the presence of an abnormal arterial pattern with a resultant decrease in collateral circulation to the lower limb places the limb at risk from a secondary teratogenic event that can result in limb malformations. This situation can potentially explain Patient 1 and Patient 2 who have a similar artery deficient bilaterally, decreased collateral flow from a deficient peroneal arterial supply, and discordant phenotypes in their left and right lower limbs. Maternal smoking increases fetal hypoxia [24], and the relation of maternal smoking to increased risk of clubfoot development [11, 23] provides further evidence for the hypoxic-induced nature of congenital lower limb deformities. Additionally, an epidemiologic study associated the presence of maternal anemia with clubfoot [3]. Induction of maternal anemia by bleeding rats resulted in congenital limb anomalies such as shortened extremities, polydactyly, and syndactyly [27].

As a research tool, magnetic resonance angiography may also be useful in characterizing the biological pathways through which gene mutations cause abnormalities in lower limb development. At least in syndromic cases, the vertical talus and clubfoot phenotypes are due to many diverse etiologies [10]. Although vascular abnormalities are common in vertical talus and clubfoot, the relatively normal vasculature in Patient 3, who has a CDMP-1 mutation known to cause familial vertical talus [5], would support the theory that multiple pathways could result in a similar phenotype. However, it will be important to determine the degree to which vascular anomalies are consistent in individuals with identical gene mutations. Evaluation of vascular anomalies in seemingly unaffected members of a large kindred with clubfoot may also aid gene discovery as better classification of potential carriers of the disorder may improve the power of genetic linkage studies.

With additional vascular characterization of large numbers of patients, magnetic resonance angiography may become an important diagnostic test. It has already been suggested that tissue necrosis seen as a complication of extensive soft tissue release surgery for clubfoot is related to the increased metabolic demands of wound healing superimposed on a postsurgical foot with an arterial deficiency [4]. Further research studies are needed to determine whether vascular anomalies are associated with higher complication or recurrence rates, or are markers of familial or sporadic occurrence.

Magnetic resonance angiography is a less invasive, more accurate technology allowing for further studies to elucidate the vascular structure of individuals affected with congenital limb deformities. This technology, combined with advances in genetic diagnosis, may help to determine

etiology of these conditions, advance treatment, and develop effective prevention strategies.

Acknowledgments We thank Dr. Thomas Herman and Dr. Mark Levinsohn for reviewing the MRA studies.

References

- Alaee F, Boehm S, Dobbs MB. A new approach to the treatment of congenital vertical talus. *J Child Orthop*. 2007;1:165–174.
- Ben-Menachem Y, Butler JE. Arteriography of the foot in congenital deformities. *J Bone Joint Surg Am*. 1974;56:1625–1630.
- Byron-Scott R, Sharpe P, Hasler C, Cundy P, Hirte C, Chan A, Scott H, Baghurst P, Haan E. A South Australian population-based study of congenital talipes equinovarus. *Paediatr Perinat Epidemiol*. 2005;19:227–237.
- Dobbs MB, Gordon JE, Schoenecker PL. Absent posterior tibial artery associated with idiopathic clubfoot. A report of two cases. *J Bone Joint Surg Am*. 2004;86:599–602.
- Dobbs MB, Gurnett CA, Robarge J, Gordon JE, Morcuende JA, Bowcock AM. Variable hand and foot abnormalities in family with congenital vertical talus and CDMP-1 gene mutation. *J Orthop Res*. 2005;23:1490–1494.
- Dobbs MB, Purcell DB, Nunley R, Morcuende JA. Early results of a new method of treatment for idiopathic congenital vertical talus. *J Bone Joint Surg Am*. 2006;88:1192–1200.
- Dobbs MB, Purcell DB, Nunley R, Morcuende JA. Early results of a new method of treatment for idiopathic congenital vertical talus. Surgical technique. *J Bone Joint Surg Am*. 2007;89 Suppl 2 Pt.1:111–121.
- Edelson JG, Hussein N. The pulseless clubfoot. *J Bone Joint Surg Br*. 1984;66:700–702.
- Greider TD, Siff SJ, Gerson P, Donovan MM. Arteriography in clubfoot. *J Bone Joint Surg Am*. 1982;64:837–840.
- Gurnett CA, Boehm S, Connolly A, Reimschisel T, Dobbs MB. Impact of congenital talipes equinovarus etiology on treatment outcomes. *Dev Med Child Neurol*. 2008;50:498–502.
- Honein MA, Paulozzi LJ, Moore CA. Family history, maternal smoking, and clubfoot: an indication of a gene-environment interaction. *Am J Epidemiol*. 2000;152:658–665.
- Hootnick DR, Levinsohn EM, Crider RJ, Packard DS Jr. Congenital arterial malformations associated with clubfoot. A report of two cases. *Clin Orthop Relat Res*. 1982;167:160–163.
- Hootnick DR, Levinsohn EM, Randall PA, Packard DS Jr. Vascular dysgenesis associated with skeletal dysplasia of the lower limb. *J Bone Joint Surg Am*. 1980;62:1123–1129.
- Husain T, Langlois PH, Sever LE, Gambello MJ. Descriptive epidemiologic features shared by birth defects thought to be related to vascular disruption in Texas, 1996–2002. *Birth Defects Res A Clin Mol Teratol*. 2008;82:435–440.
- Katz DA, Albanese EL, Levinsohn EM, Hootnick DR, Packard DS Jr, Grant WD, Mann KA, Albanese SA. Pulsed color-flow Doppler analysis of arterial deficiency in idiopathic clubfoot. *J Pediatr Orthop*. 2003;23:84–87.
- Kitziger K, Wilkins K. Absent posterior tibial artery in an infant with talipes equinovarus. *J Pediatr Orthop*. 1991;11:777–778.
- Levinsohn EM, Hootnick DR, Packard DS Jr. Consistent arterial abnormalities associated with a variety of congenital malformations of the human lower limb. *Invest Radiol*. 1991;26:364–373.
- Ponseti IV. *Congenital Clubfoot: Fundamentals of Treatment*. 1st ed. Oxford: Oxford University Press; 1996.
- Poswillo D. The pathogenesis of the first and second branchial arch syndrome. *Oral Surg Oral Med Oral Pathol*. 1973;35:302–328.

20. Quillin SP, Hicks ME. Absent posterior tibial artery associated with clubfoot deformity: an unusual variant. *J Vasc Interv Radiol*. 1994;5:497–499.
21. Sarrafian SK. *Anatomy of the Foot and Ankle: Descriptive Topographic Functional*. 2nd ed. Chicago, IL: JB Lippincott Co; 1993.
22. Shah DJ, Brown B, Kim RJ, Grizzard JD. Magnetic resonance evaluation of peripheral arterial disease. *Magn Reson Imaging Clin N Am*. 2007;15:653–679, vii.
23. Skelly AC, Holt VL, Mosca VS, Alderman BW. Talipes equinovarus and maternal smoking: a population-based case-control study in Washington State. *Teratology*. 2002;66:91–100.
24. Socol ML, Manning FA, Murata Y, Druzin ML. Maternal smoking causes fetal hypoxia: experimental evidence. *Am J Obstet Gynecol*. 1982;142:214–218.
25. Sodré H, Bruschini S, Mestriner LA, Miranda F Jr, Levinsohn EM, Packard DS Jr, Crider RJ Jr, Schwartz R, Hootnick DR. Arterial abnormalities in talipes equinovarus as assessed by angiography and the Doppler technique. *J Pediatr Orthop*. 1990;10:101–104.
26. Sodré H, Lourenço A, Amorim J. Arteriografia no pé talo vertical congénito. *Rev Bras Ortop*. 1995;30:39–41.
27. Webster WS, Abela D. The effect of hypoxia in development. *Birth Defects Res C Embryo Today*. 2007;81:215–228.