Hemihypertrophy

Matthew Minor, M.D., and David Wang, D.O.
Department of Diagnostic Imaging, Wilford Hall Ambulatory Surgical Center, San Antonio, TX

Case Presentation
A 54-year-old woman with a port wine stain since childhood presented with hypertrophy of the left lower extremity. She has been wearing compression stockings for painful swelling of the left lower extremity since childhood. In addition, she walks with a limp secondary to the left side of her pelvis "riding higher" than the right.

Figure: Axial fat suppressed T2 (A) and T1 (B) weighted images of the lower extremities demonstrate asymmetric enlargement of the left calf with lipomatous hypertrophy and prominent vasculature compared with the right.
Key clinical finding(s)
Cutaneous vascular nevus
Unilateral lower extremity hypertrophy

Key imaging finding(s)
Unilateral extremity lipomatous hypertrophy and vascular ectasia

Differential diagnoses
Klippel-Trénaunay Syndrome
Parke-Weber Syndrome
Neurofibromatosis
Maffucci Syndrome
Macroductrophia lipomatosa
Proteus Syndrome

Discussion
Gigantism (focal or diffuse), macromelia, macrodactyly, and hemihypertrophy are all terms referring to enlargement of all or a part of the body. Specifically, hemihypertrophy is asymmetric enlargement or overgrowth of one side of the body with hypertrophy of the muscles, blood vessels, nerves, and bones. Enlargement of one portion of the body can be seen in a number of congenital and developmental conditions for which clinical history and physical exam will aid in the differential diagnosis.

Klippel-Trénaunay Syndrome:
First described in 1900, Klippel-Trénaunay Syndrome consists of three physical findings: cutaneous vascular nevus (capillary malformation), soft tissue or bony hypertrophy of the extremity, and varicose veins or venous malformations. A diagnosis of Klippel-Trénaunay requires two of the three findings. This rare anomaly only occurs in 1 of 20,000 to 40,000 live births. The cause of the disease is poorly understood.

Clinically, patients with Klippel-Trénaunay Syndrome have vascular abnormalities such as superficial pigmented hemangiomas (port-wine nevus or nevus flammeus), varicose veins, lymphangiomas, and a deficient deep venous system. Limb deformity is usually monomelic with local gigantism developing early in childhood and involving all or a portion of a limb. Asymmetry is variable and may be due to either soft-tissue (muscular or lipomatous) or osseous overgrowth. The vast majority of cases involve the lower limbs. On MRI, soft-tissue asymmetry can be appreciated with bilateral imaging of the extremities.

Venous anomalies have classically been imaged with CT venography and more recently with MRI. Abnormalities of the venous system range from simple ectasia of the superficial and deep system, including varicosities, to persistent fetal veins and large venous malformations. The presence of a sciatic vein has been well documented as a common finding in Klippel-Trénaunay Syndrome.

Parke-Weber Syndrome:
In 1907, Parke-Weber described a number of cases that involved the classic findings of Klippel-Trénaunay Syndrome with one important addition - arteriovenous fistulas. Over the years, many authors have simply combined these two syndromes into Klippel-Trénaunay-Weber Syndrome; however, the distinction between the two groups can be determined through arteriography.

Neurofibromatosis:
Neurofibromatosis type 1 (NF1) is the most common neurocutaneous disease. Also, known as von Recklinghausen disease, NF1 is characterized by neurofibromas, café au lait spots, gliomas, and skeletal dysplasia. Overgrowth of bone and soft tissue can result in elephantoid soft tissue hypertrophy of a part of or a whole extremity. Physical exam and clinical history are strong discriminators.

Maffucci Syndrome:
Maffucci Syndrome is a condition within the spectrum of multiple enchondromatosis characterized by enchondromatosis and soft tissue hemangiomias. The disease affects tubular bones, most commonly in the hands. Asymmetric nodular enlargement of the affected limb results in local gigantism. Radiographic examination will show pathognomonic phleboliths from the vascular lesions and multiple bony lytic lesions with a chondroid matrix, typical of enchondromas. The presence of enchondromas is a discerning feature.
Beckwith Weidemann Syndrome:
Beckwith Wiedemann Syndrome is an autosomal dominant disorder characterized by local gigantism, macrosomia, and hemihypertrophy. Associated anomalies include macroglossia, otic dysplasia, omphalocele, cardiac anomalies, and organomegaly (kidney, liver, and spleen). There is a high risk for the development of neoplasia, including Wilms tumor, adrenocortical carcinoma, neuroblastoma, and hepatoblastoma, among others.

Macrodystrophia Lipomatosa:
Macrodystrophia lipomatosa is a developmental anomaly predominantly affecting fingers and toes characterized by overgrowth of all the tissues of mesenchymal origin, predominantly involving fibroadipose tissue. Its cause is unknown. Unilateral involvement is typical with overgrowth more pronounced distally. There is no gender predilection and the deformity can be seen at birth or early infancy, progressing until puberty. Other deformities such as syndactyly, clinodactyly and polydactyly can be associated with macrodystrophia lipomatosa.

Proteus Syndrome:
In 1960, Proteus syndrome was described, consisting of partial gigantism of the hands and/or feet, hemihypertrophy, pigmented nevi, subcutaneous ‘tumors,’ skull anomalies, accelerated growth, and visceral abnormalities. A hallmark of this syndrome is its mosaic pattern of involvement. Diagnostic criteria and guidelines include skeletal surveys; MRI evaluation of the abdomen, pelvis, and central nervous system; and CT evaluation of the chest. Recently, researchers determined that a variant of the AKT1 (protein encoding gene) is the cause of the Proteus syndrome.

Summary
Hemihypertrophy or unilateral asymmetric gigantism is a rare condition, which may arise from a variety of congenital and developmental conditions. Aside from known syndromes, the initial presenting symptom is often a limb length discrepancy. Clinical assessment, associated anomalies, and imaging findings help differentiate these rare conditions from one another. As seen with this case, MRI findings of venous abnormalities and limb hypertrophy are characteristic and readily evident in the setting of Klippel-Trénaunay Syndrome.

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References