MACRODACTYLY, HEMIHYPERPLASIA, AND THE DYSMORPHIC FIRST RAY

Carl A. Kihm, DPM
Craig A. Camasta, DPM

INTRODUCTION

Congenital overgrowth disorders of the lower extremity have been rarely reported in podiatric literature. Since the 1980s, however, advancements in genetics and diagnostic imaging have allowed for a better understanding of these conditions. The etiologies of overgrowth conditions are largely unknown. Although overgrowth conditions are highly variable, clinically, these patients present similarly with difficulty in walking, fitting in shoes, toenail irritation, and cosmetic concerns. Conservative treatment is often of limited long-term value. Surgical intervention must be approached on a case-specific basis with attention to multiple factors. Due to the rarity of these conditions, large studies are lacking and most of our knowledge and surgical recommendations are based off of case studies. In this update, we will review these conditions and clarify the differences among them. We present a patient with an overgrowth condition of the first ray and describe the surgical correction that yielded a successful outcome.

MACRODACTYLY

Literal translation of the term, macrodactyly is "large digit." As the name implies, macrodactyly usually presents as overgrowth of an entire digit. Other names for this condition are localized hypertrophy, local gigantism, and megalocatyly (1). True macrodactyly involves hypertrophy of all the structures of the digit: the skin, toenail, subcutaneous fat, bones, nerves, and blood vessels (1-3). False macrodactyly presents as hypertrophy of primarily one tissue type (4).

Macrodactyly affects the fingers more frequently than the toes (5, 6), with concurrent upper and lower extremity involvement being extremely rare (7). See Figure 1. In the foot, macrodactyly usually presents in the first, second or third digit (1); the second digit is most frequently involved (8, 9). When overgrowth of an adjacent digit is also present, syndactyly is not unusual (3, 4).

Etiology for macrodactyly remains unknown, however, heredity does not appear to play a major role (2, 3, 10). Macrodactyly has been suspected to be the result of

neurofibromatosis (1). The incidence of macrodactyly in an active pediatric orthopedic clinic has been reported as 0.035%, with a slight male predominance (male:female= 1.2:1) (8).

Two forms of macrodactyly have been defined – static and progressive (3, 11). The static form usually presents at birth with a noticeable overgrowth that enlarges proportionally throughout development. The progressive form of the deformity may also appear at birth but the digit undergoes a rapid, disproportional growth that results in a grotesque deformity (1, 4). Involvement of hypertrophy proximal to the metatarsophalangeal joint is rare in the static form but common in the progressive form (1, 4). The respective metatarsal is involved in about half of all cases (8).

Macrodactyly usually presents as an isolated condition (12, 13), however, it can present as an associated condition. True macrodactyly is associated

Figure 1. Macrodactyly. This overgrowth condition can affect one or multiple digits of the upper or lower extremities. Fingers are involved more frequently than toes. The deformity can present unilaterally or bilaterally.

Table 1

CONDITIONS ASSOCIATED WITH MACRODACTYLY

Subtype	Associated Condition	Distinguishing Features
"True" Macrodactyly	Proteus syndrome	Connective tissue nevi, epidermal nevi, disproportionate growth
"False" Macrodactyly	Oiller's disease	Enchondromatosis, cerebral tumors
	Maffucci's syndrome	Enchondromatosis, hemangioma
	Milroy's disease	Congenital lymphedema
	Klippel-Trenauny syndrome	Port wine hemangioma, varicose veins, soft tissue/bone hypertrophy
	Vascular malformation	
	Neurofibromatosis	

with Proteus syndrome, which is a rare disorder of skeletal, hamatomatous, and mesodermal malformations (14). Proteus syndrome has a mosaic distribution and sporadic occurrence (15). In addition to unilateral disproportionate overgrowth, other characteristic features include connective tissue nevi, dysregulated adipose tissue, and vascular malformation (15). Macrodactyly associated with Proteus syndrome should be differentiated from isolated macrodactyly because of its progressive nature, poor prognosis and high associated rates of recurrence (16). False macrodactyly has been associated with a variety of pathologies, including Ollier's disease, Maffucci's syndrome, vascular malformation, neuro-fibromatosis, and Milroy's disease (17) (Table 1).

HEMIHYPERPLASIA

Hemihyperplasia describes a heterogeneous group of disorders that present with a unilateral overgrowth that can affect structures of the head, trunk, and/or extremities, with or without visceral involvement (18, 19). The term, hemihyperplasia, literally means "half overgrowth." This condition is synonymously known as true hypertrophy, hyperplasia, hemigigantism, partial macrosomia, mega-losomia, and congenital hemicorporal disharmony (19). As the appropriately named term hyperplasia denotes, these overgrowth conditions are the result of abnormal cell proliferation (18, 20). Overgrowth caused by hyperplasia is different from hypertrophy, a condition in which a normal number of cells increase in size (18, 20).

Asymmetry at birth is almost always evident (19) and the enlarged side generally develops proportionally to the uninvolved side (21). Unlike macrodactyly, hemihyperplasia overgrowth is not limited to a digit or a ray. Overgrowth in both length and circumference (18) of the entire foot or the entire lower extremity present a more challenging

Table 2

POSSIBLE CAUSES OF ACQUIRED AND CONGENITAL FORMS OF HEMIHYPERTROPHY

Subtype	Extent of Condition
Congenital Hypertrophy	Total (involving all systems)
	Segmental
	Crossed
	Hemihypertrophy
	Limited Hypertrophy (one or more systems are involved)
	Mucsular
	Vascular
	Skeletal
	Neurologic
Acquired Hypertrophy	Total Hypertrophy
	Gigantism - Hyperpituitarism
	Neurofibromatosis
	Limited Hypertrophy
	Milroy's disease
	Elephantiasis
	Lipomatosis
	Neuro
	Vascular anomalies
	Multiple arteriovenous aneurysms

(Modified from: Wagreich CR. Congenital deformities. In: AS, Downey MS, Martin DE, et al. McGlamry's Forefoot Surgery, 1st Edition. Lippincott Williams & Wilkins; 2004:487-511.)

condition. Unilateral limb overgrowth results in a limb-length discrepancy that can lead to pelvic tilt and scoliosis (18).

The incidence of isolated hemihyperplasia has been reported to be 1:86,000 live births (22). Females are twice as likely to be affected as males (23), and right-sided overgrowth is more frequent (right:left=1.36:1.00) (18).

Hemihyperplasia conditions are highly variable so further classification is helpful to describe the extent of overgrowth. As shown in Table 2, hemihyperplasia overgrowth can be congenital or acquired and have total or limited involvement. Isolated hemihyperplasia usually presents with a mild overgrowth, which is stable during infancy and adolescence (24). Hemihyperplasia can also be associated with a variety of other malformation syndromes (18) (Table 3). Poor prognosis and reduced long-term survival is generally expected when hemihyperplasia presents as an associated condition (18). Patients with isolated hemihypertrophy usually have an average lifespan (18). In 1998, Hoyme reported a 5.9% incidence of tumors in patients with hemihyperplasia; Wilms tumor, hepatoblastoma, and adrenal cell carcinoma were most frequently reported (18). The authors believe the embryonic nature of the tumors associated with overgrowth and neoplasm may suggest a common mechanism for uncontrolled cell proliferation (18).

Table 3

CONDITIONS ASSOCIATED WITH HEMIHYPERTROPHY

Syndrome	Features
Wiedmann-Beckwith	Omphalocele, hypoglycemia, generalize overgrowth, macroglossia, predisposition to neoplasia
Neurofibromatosis	Café-au-lait spots, hypopigmented patches, neurofibromas, macrocephaly, CNS tumors
Klippel-Trenaunay-Weber	Hemangiomata, lymphatic abnormalities, polydactyly, syndactyly, glaucoma, cateracts
Proteus syndrome	Connective tissue nevi, lipomata, hemangiomata, macrocephaly, scoloiosis
Epidermal nevus	Pigmentary changes, mental deficiency, seizures, CNS malformations, potential for malignancy
Mafucci's syndrome	Enchondromata, hemangiomata, bowing of long bones, chondromsarcoma
Ollier's disease	Bilateral, asymmetric enchondromata, fractures, chondrosarcoma

Conditions Associated with Hemihypertrophy.(Modified from: Hoyme HE, Seaver LH, Procopio F, et al. Isolated hemihyperplasia (hemihypertrophy): report of a prospective multicenter study of the incidence of neoplasia and review. Am J Med Genet 1998;79:274-8.)

Recently, molecular genetics studies have provided insight to the etiology of hemihyperplasia. Overexpression of the insulin-like growth factor 2 (IGF2) gene has been implicated to cause isolated hemihypertrophy and other manifestations of Wiedemann-Beckwith syndrome (18). In 2010, Ricks identified duplications involving a 1.65 Mb critical region on chromosome Xq25 to be significant for hemihyperplasia and digital anomalies (25). Comparative genome hybridization studies on patients with hemi-hyperplasia could identify Xq25 duplications; this would dramatically change recurrence risk estimations and provide insight into comorbidities (25).

DYSMORPHIC FIRST RAY

Overgrowth conditions have been recognized for thousands of years, but the concept of the dysmorphic first ray has been largely overlooked. Camasta's morphometric analysis on size and shape of lesser tarsus bone specimens demonstrated the analogous form of the first ray to the lesser digits (26) (Figure 2). The joints of the three bones of the first ray experience the same forces as the three bones comprising lesser digits. Thus, Camasta has defined hallux limitus to be analogous to the lesser digit hammertoe deformity (27) (Figure 3). Further, morphometric analysis allowed Camasta to deduce that bones of the first ray are embryologically analogous to the bones of the lesser digits. Bone length and width patterns support this claim. A consistent 0.75:1.0:2.0 ratio of bone length patterns (distal:middle:proximal segment) has been described in the first ray (hallux distal phalanx, hallux proximal phalanx, and first metatarsal) and
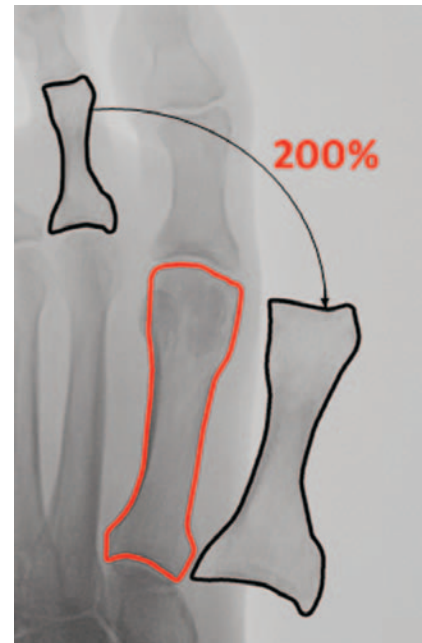

Figure 2. The First Ray is Analogous to the Second Digit. When the proximal phalanx of the second digit is scaled to 200%, the shape of the bone (length and width) closely resembles the first metatarsal.
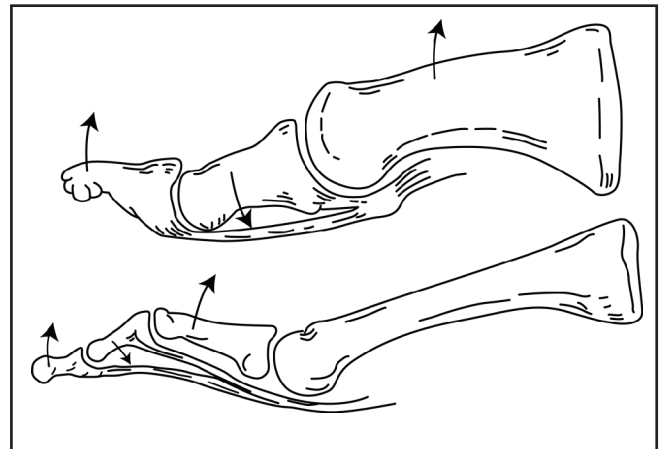

Figure 3. Hallux Limitus is Analogous to the Hammertoe Deformity. The concept of the first ray being analogous to the second digit is validated clinically by understanding the analogous positional changes in hallux limitus and hammertoe deformities. The distal joint is dorsiflexed and the proximal joint is plantarflexed similarly in both deformities. (Image from: Camasta CA. Hallux limitus and hallux rigidus. clinical examination, radiographic findings, and natural history. Clinics Pod Med Surg 1996; 13(3):423-48.)

the second digit (distal, middle, and proximal phalanges) (26) (Figure 4). Normal radiographic measurements in subsequent morphometric reports (28) support this claim by having similar bone length patterns. Significant deviation from these length ratios can result in clinical manifestations. Disproportionate aberrations found in the first ray may not always be pathological. Past authors have associated length
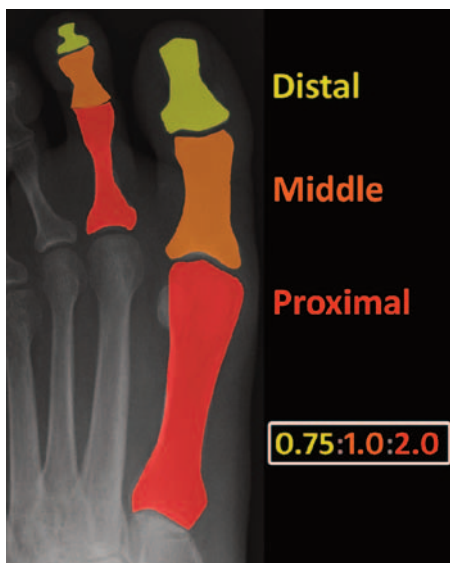
Figure 4. Bone Length Ratios of the First Ray and Second Digit. Camasta's morphometric analysis suggests the analogous first ray and second digit consistently have segments of the same proportions. The bone length ratio of 0.75:1.0:2.0 describes the lengths of the distal:middle:proximal segments. Aberrations in the length ratios reveal a dysmorphic condition.

pattern aberrations of the first ray with hallux limitus, hallux abducto valgus, and hallux varus (29-33). A clinically elongated or shortened first ray or lesser digit requires calculation of the bone segment's relative length ratio to identify the presence and location of a dysmorph. One long bone segment or multiple long segments can result in a gross overgrowth condition. Knowledge of normal length ratios and then identification of a dysmorphic segment are helpful in planning surgical correction (34).

The most common form of dysmorphic first ray is symmetrical macrodactyly, where all three segments are enlarged proportionately to the normal scaling parameters (0.75:1.0:2.0). A mild form of symmetrical macrodactyly can be seen in patients with a hallux valgus deformity, and failure to recognize this may lead to under or overcorrection of the condition. Congenital macrodactyly of the first ray tends to produce a congenital or developmental hallux varus. The next most common form of dysmorphic first ray is a short proximal phalanx, and most of these patients have hallux limitus/rigidus.

DIAGNOSIS

In general, some overgrowth conditions present as a subtle clinical finding, while others are grossly apparent. Once recognized, a focused history and clinical evaluation are required to determine the extent and severity of the overgrowth condition. Associated conditions should also be noted and appropriate consultations should be made as necessary.

If the overgrowth is limited to a digit or ray, macrodactyly may initially be suspected. Often, however, an enlarged digit will be incorrectly diagnosed as macrodactyly (3), so a focused examination is required with consideration of differential diagnoses. History of trauma may be suggestive of hematoma (3). Radiographs and computed tomography (CT) can differentiate from an osseous neoplasm. Soft tissue neoplasms are best assessed via magnetic resonance imaging (MRI) (35, 36). MRIs and radiographs also allow for assessment of the tissue type and consistency of an overgrowth (35). Thus, these imaging techniques are useful in differentiating true from false macrodactyly. Macrodactyly may present unilaterally or bilaterally, and symmetrically or asymmetrically; a bilateral condition can be differentiated from hemihyperplasia, which is unilateral, by definition (1, 3). A thorough history, provided by the young patient's parents, should be acquired. The initial presentation of the condition and the course of progression can indicate whether a macrodactyly is of the static or progressive form. Circumferences and lengths of the involved and uninvolved sides allow for relative size comparisons. These measurements can be assessed over the course of subsequent office visits. This helps verify the deformity as the static or progressive form. If progressing, the measurements can be used to calculate the rate of progression.

Hemihyperplasia should be considered in patients presenting with unilateral lower extremity asymmetry with or without asymmetry of the head, trunk, or viscera. This is a diagnosis of exclusion (18). Differentials must be ruled out for lymphatic disorders, vascular malformation, hemangioma, bone dysplasia, and arteriovenous malformation (19). In these patients, overgrowth can involve the entire foot or limb.

Dysmorphia of the first ray or lesser digit is diagnosed by clinical and radiographic examination. Radiographic evaluation of a clinically enlarged digit should include length measurements of each bone segment comprising the affected area. Length ratios should be calculated and compared to that of the contralateral side or the normal ratio of 0.75:1.0:2.0, described above. In the dysmorphic presentation, overgrowth of one or two bones comprising the involved segment may be responsible for what clinically appears as macrodactyly.

When evaluating overgrowth malformations, it is also important to rule out hypoplasia of the adjacent digits or contralateral parts. As shown in Figure 5, premature arrest of

Figure 5. Hemihypoplasia: Differential for Overgrowth. A digit may appear enlarged if nearby structures are abnormally small. In this example, the first, third and fourth metatarsals are abnormally small due to premature closure of the growth plates. The second digit initially appears to be an overgrowth, however, it is actually of normal size.

the growth plates in the first, third, and fourth metatarsals give the clinical appearance of a large second metatarsal. In this case, the relatively large metatarsal was normal and not an overgrowth deformity. The same consideration should be made when evaluating a unilateral overgrowth of the entire foot or limb.

TREATMENT

Treatment for each patient presenting with an overgrowth condition should be decided on an individualized basis. The type and subtype of the condition, the patient's age, the extent of deformity, and limitation caused by the deformity should be factored (1, 3). Foot lifts, padding, customized shoes, and other conservative treatments may be somewhat beneficial; however, they often provide only limited long-term relief (9). Surgery for these conditions is the primary treatment (19) and should be approached with the goals of improving ambulation, and obtaining a painless, plantargrade foot that is cosmetically acceptable and can fit into a shoe (1, 9, 17, 19). Unfortunately, due to the rarity of the overgrowth conditions, there are limited large, long-term studies to provide surgical treatment guidelines.

The overgrowth condition, the form of the condition, and the presence of associated conditions should be considered. In macrodactyly, the static form is likely to have

a good outcome after shortening and soft tissue debulking (1). Complete or partial digit or ray amputation has been advocated in severe deformity (2). Progressive macrodactyly is reported to be more difficult to treat. Perdiue warned that treatment of progressive macrodactyly uniformly leads to unsatisfactory outcomes (1). In progressive macrodactyly, the majority of the overgrowth oftentimes involves the distal and plantar tissues (1, 19), so the toe appears hyperextended (3). Even an amputation may not necessarily stop overgrowth of fatty tissue proximal to the amputation site (3, 9). Overgrowth of the metatarsal can be managed via a shortening osteotomy through the metatarsal's metaphyseal bone (9). Unfortunately, recurrence and need for additional surgery, prolonged edema, and wound healing problems can occur (9). Wound healing issues may be the result of altered circulation (1, 19). Staging osseous and soft tissue surgical procedures has therefore been suggested (37). Healing typically occurs, although at a slow rate, and amputation is not required (1). Because young children have less wound healing issues, some advise early surgical intervention (19, 38). Chang delayed surgery until the child was at least six months old and usually performed surgery before the age of 2 years (9). Hop also recommended early intervention but noted that these surgeries are often delayed because surgeons are unfamiliar with these conditions and lack experience in treating them (17).

Epiphysiodesis via growth plate destruction, stapling, or wiring (3) has been suggested in children younger than 10 years (9, 19). The goal is to restore the proportionality of the digits by arresting the overgrowth (1). In pedal macrodactyly, epiphysiodesis is unpredictable, thus, it is not recommended as an isolated procedure (1).

Chang suggested digital amputation if the digit was twice the size of the contralateral side (9). Foot widening, seen in macrodactyly or hemihyperplasia, may also necessitate resection of wedge osteotomies (1, 3, 9, 19). When foot length and width are still not adequate, ray resection is suggested (9). In feet with less severe deformity, shortening osteotomies with or without joint arthrodesis have been described (9). Arthrodesis of the first metatarsophalangeal joint or hallux interphalangeal joint, or the lesser digit's proximal or distal interphalangeal joints may be indicated depending on the extent of overgrowth (3, 38). Unsdorfer reported satisfactory long-term results upon proximal phalanx base resection for multi-planar digital deformities (39). Other approaches have been specifically designed to allow for toenail preservation when performing shortening osteotomies or debulking (1, 3, 38, 40).

CASE STUDY

A 19-year-old African American female presented with the chief complaint of a large hallux that made fitting in shoes difficult (Figure 6). The patient was a college student but was unable to participate in many activities due to difficulty with walking. The patient's medical history was unremarkable for congenital abnormalities and associated conditions. She reported that the toe had been large since birth and it progressively got larger as she got older. At the time of presentation, she reported the toe has been stable, with no growth, for the past 5 years. Her over-growth deformity was not a painful condition, but it caused her cosmetic and functional problems that led her to seek surgical correction.

Her unilateral, static overgrowth was assessed via radiographic and MRI modalities to gain more information (Figure 7). The overgrowth was isolated to the first ray and involved all bone segments. Calculation of length ratios revealed the deformity to be a symmetrical macrodactyly of the first ray. Clinically, crepitus at the hallux interphalangeal joint correlated with a plantar osteochondroma at the base of the hallux distal phalanx. A large fibrolipomatous hemartoma of the plantar hallux was found to be composed of dense homogenous tissue on MRI. The osteochondroma and hemartoma are features associated with false macrodactyly and hemihyperplasia.

Surgery was approached in a staged fashion. The purpose of the first procedure was to shorten the bone segments of the first ray. The distal phalanx tuft and osteochondroma were removed. The hallux interphalangeal joint was aggressively resected to achieve shortening prior to joint arthrodesis. A double chevron osteotomy in the first metatarsal head was also performed to effectively shorten this bone segment. Minimal soft tissue resection was performed initially. By preserving blood supply, the arthrodesis and osteotomy would theoretically have a greater healing potential. After six months, the bone healed (Figure 8) and a second surgery was performed to aggressively debulk the excess soft tissues. Excess dorsal skin was excised and the toenail was preserved.

The patient healed well without complication or recurrence. Two years following surgery, the patient is still very satisfied with her cosmetic and functional outcome (Figure 9). Her shoe size changed from size 11 wide to size 8.5 regular.

Figure 6. Preoperative Clinical Presentation. Gross enlargement of the first ray is evident. The plantar fibrolipomatous overgrowth mass causes the hallux distal phalanx to be dorsiflexed. The toenail is angled and this can cause irritation.

Figure 7. Radiographic and MRI Images. Measurements of each bone segment revealed a proportional increase in size of each bone in the first ray, consistent with symmetrical macrodactyly. A plantar osteo-chondroma was noted at the base of the hallux distal phalanx. On MRI, the hemartoma was noted to be homogenous.

Figure 8. Postoperative Outcome. Two years after the staged procedures, the patient has an improved functional outcome. She has a better cosmetically-appearing first ray that she can fit into her shoe. No complications or recurrence have occurred.

Figure 9.

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