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Schmid Type Metaphyseal Chondrodysplasia in a Large Single Genetic Lineage

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Abstract

Several subtypes of metaphyseal chondrodysplasia exist, of which the Schmid type is the most common. Characteristics include short limbed dwarfism, coxa vara, genu vara, and waddling gait. Skull, spine, and upper extremity involvement is minimal and often nonexistent. The primary defect involves a mutation affecting the metaphyseal portion of the growth plate, while the epiphysis is normal. A large single lineage family with metaphyseal chondrodysplasia, Schmid type (MCDS) was investigated. A genetic pedigree of 135 members of this family showed autosomal dominant inheritance between all 42 affected members. The large sample size allowed for the characterization of a broad range of features present in cases of MCDS. The majority of affected patients exhibited coxa vara with an average neck/shaft angle of 105 degrees. Despite coxa vara, premature osteoarthritis of the hip is not a feature of MCDS. Genu varum is the most prevalent knee disorder in this group, but greater than 30% of patients may exhibit genu valgum. This manuscript highlights MCDS background information, differential diagnoses, treatment options, and prognosis to aid in clinical decision-making.

Introduction

Metaphyseal chondrodysplasias (MCD) represent an array of conditions that present complex challenges for orthopaedic surgeons, as potentially, all long bones can be affected in unison.[1] Radiographs reveal irregularities including splaying, flaring, cupping, and shortening of the tubular long bones with widened epiphyseal plates. Widespread coxa vara results in the quintessential waddling gait seen in patients (Figure 1). Sclerosis, and less commonly, vertebral platyspondyly and hand involvement may be present. In addition, joint pain has been reported in the past.[2]

Schmid metaphyseal dyschondroplasia (MCDS) is an inherited metaphyseal disorder first described in 1949.[3] Historically, MCDS was radiographically characterized by irregularities of the long-bone metaphases with normal hand and vertebral development.[4] Spine involvement was evident in scattered cases, but often resolved as patients aged.[5] Today, MCDS is described as the development of progressive short stature with features usually absent at birth. Clinical characteristics manifest in early childhood with short limbs, genu varum, and waddling gait (Figure 2). Facial features and head size are typically normal, but adult height is several standard deviations below the mean, with a wide spectrum throughout affected individuals. Extraskeletal manifestations are absent, and affected individuals display normal intelligence.[2]

MCDS is caused by a mutation of the *COL10A1* gene, which is transmitted in an autosomal dominant mode of inheritance. This

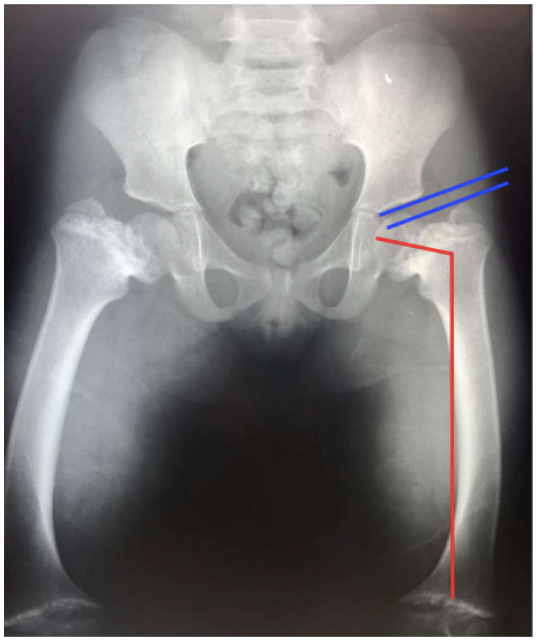

Figure 1. AP radiograph of pelvis and proximal femur in a known MCDS patient. The typical decreased neck-shaft angle (coxa vara) is seen (red). Furthermore, decreased articulo-trochanteric distance (distance between tangential lines about the superior acetabular articular surface and superior pole of the greater trochanter) accompanies the coxa vara deformity (blue). Splaying and flaring of the growth plates is evident.

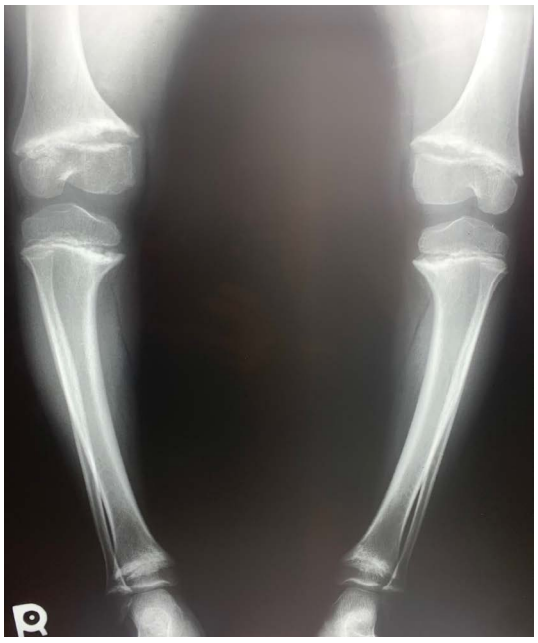

Figure 2. AP radiograph of knee and tibia in a known MCDS patient. Genu varus with irregularities in the growth plates can be seen bilaterally.

mutation quantitatively reduces collagen type X production, thereby reducing its presence at the hypertrophic zone adjacent to calcifying cartilage.[1] Endochondral ossification, the process by which long bones elongate, is ultimately obscured. It is also the most common of the inherited metaphyseal chondrodysplasias, occurring at an estimated rate of three to six cases per million, which some current authors believe is a profound underestimation.[6,7]

Other, rarer metaphyseal chondrodysplasias with similar features to those of MCDS should be considered among the differential diagnoses. These include Jansen type, McKusick type (Cartilage–Hair Hypoplasia –CHH), and MCD with Malabsorption and Neutropenia (Shwachman Diamond Syndrome –SDS). CHH and SDS have additional multi-system involvement. Meticulous assessment of the patient, including judicious scrutiny of radiographs and analysis of complete laboratory markers, is crucial to avoid misdiagnosing these complex conditions with rickets.[8]

Regarded as the most severe subtype, Jansen metaphyseal chondrodysplasia (JMC) is a rare autosomal-dominant disease caused by activating mutations of *PTHR1* resulting in inhibition of chondrocyte hypertrophic differentiation.[6,9] Features of this disorder are more profound than those of MCDS and are detected at birth.[6] In infancy, osteopenia, subperiosteal erosions, and hypercalcemia may cause confusion with hyperparathyroidism.[10] Patients exhibit marked growth plate abnormalities, short stature and bowing of long bones, micrognathia, hypertelorism, and premature closure of cranial sutures.[9]

Cartilage–hair hypoplasia (CHH) is a rare autosomal recessive metaphyseal chondrodysplasia caused by mutations of the untranslated *RMRP* gene. It is characterized by short stature with a spectrum of skeletal abnormalities, fine sparse hair, and immune deficiency that can lead to recurrent infections.[11] In the newborn, the first sign is bowing of the femora which is diagnostic, with metaphyseal changes only apparent after four months of age.[12]

Similar to CHH, Shwachman Diamond Syndrome affects multiple organ systems. A mutated *SBDS* gene on chromosome 7, normally involved in ribosome biogenesis and mitotic spindle stabilization, is disrupted, leading to the disease manifestation.[13] Besides the immune, gastrointestinal, and cardiac features, SDS patients commonly exhibit skeletal abnormalities. Uniquely, these bony changes are due to failure of the columnar cartilage cells to hypertrophy.[12] The primary defects involve abnormal development of growth plates, most frequently the femoral head.[14] Other findings include rib cage abnormalities, metaphyseal dysostosis, osteopenia, and slipped capital femoral epiphysis (SCFE).[15]

Patients with metaphyseal dysmorphisms may present a challenging clinical diagnosis to healthcare providers. The differential diagnoses can be numerous, but special care must be taken to differentiate chondrodysplasias from rickets. In an attempt to reduce overall morbidity, evaluation

of calcium and vitamin D is an essential component of initial management. Vitamin D deficiency is then subcategorized into severe deficiency (<5 ng/mL), moderate deficiency (5-15 ng/mL), and insufficiency (16-20 ng/mL).[16] Recognition of metaphyseal chondrodysplasia and differentiation from rickets is essential due to contrasting clinical treatments. While vitamin D supplementation is the remedy for rickets, it may precipitate toxicity in patients with MCDS.[12,16,17]

Orthopaedic treatment in MCDS is primarily confined to the lower extremities. Regarding gait, waddling is suggested to be caused by insufficient gluteal muscles.[18] Patients have decreased articulo-trochanteric distance (ATD) resulting in decreased gluteal mechanical advantage.[19] Usually, the entire femur shows a varus bow with the clinical appearance of genu varum. In some patients, varus alignment may improve spontaneously during childhood.

Some indications for surgical correction include significant coxa vara, a triangular fragment in the inferior femoral neck, and progressive deformity. Unfortunately, recurrence of deformity with longitudinal growth is common in many patients who have undergone surgical treatment. Guided growth procedures, such as hemiepiphysiodesis using eight-plates or stapling, may improve angular deformities in some children.[20,21,22]

Much of the research regarding MCDS occurs by studying index families, thus supporting the autosomal dominant transmission hypothesis.[6] One such family has been identified by our institution, and our investigation is arguably one of the largest regarding this disease pattern in the literature.

Materials And Methods

A large, single family affected by this disorder had been noticed by our institution when the orthopaedic surgery department began rendering services to the state Children's Rehabilitation Service (previously Crippled Children's Clinic). Forty-two members of this family exhibited MCDS and underwent a thorough history, physical exam, as well as radiographic follow-up for a minimum of twenty years All affected members manifested radiographic signs of MCDS. There were no breaks in the hereditary link or skipped generations. There was no history of consanguinity in the family.

The following clinical measurements were obtained on each affected individual of the family: standing height, sitting height, arm span length, angulation of the knee, and hip range of motion (Table 1). Normal height was established using data from the National Health Survey

Table 1. Age, sitting/standing height, arm length, knee alignment, and radiographic characteristics of the 42 family members with MCDS evaluated in the study. Comments refer to relevant orthopaedic procedures undergone by patients prior to the study.

No.	Name Age/Sex	Height Standing (in/cm)	P	Sitting Height (in/cm)	P	Arm Span (in/cm)	Knee Alignment	Hip Internal Rotation		Hip External Rotation		Hip Abduction		Neck Shaft Angle		Comments
								R	L	R	L	R	L	R	L	
1	M.S. 60+1 F	55 139.7	0	32 81.28	0	56.5 143.51	Varus	0	15	20	5	25	15	80	90	
2	I.K. 68+4 M	62.5 158.75	0	34 86.36	0	62 157.48	Valgus	0	5	35	30	30	28	135	135	
3	J.K. 63+8 M	59 149.86	0	33 83.82	0	63 150.02	Varus	13	9	40	30	30	35	100	120	
4	C.K. 48+1 M	59.5 151.13	0	32 81.28	0	60 152.14	Valgus	5	23	35	27	30	30	110	110	
5	M.K. 60+10 M	64.5 163.83	2	34 86.36	0	72.5 184.15	Straight	15	15	50	50	35	35	105	110	
6	E.M. 60+10 M	48.5 123.2	0	26.5 67.3	0	53 134.6	Valgus	40	27	15	26	35	32	100	105	
7	A.S. 30+11 F	60.75 154.31	7	33 83.82	10	53.25 158.11	Straight	30	30	30	30	30	20	90	90	
8	E.C. 38+6 F	58 147.32	0	31.5 80.01	0	60 152.4	Valgus	27	27	30	40	30	20	95	95	
9	A.R. 29+7 F	61.5 156.21	10	33 83.82	10	65 165.1	Valgus	10	10	55	55	25	25	100	100	
10	C.S. 44+6 M	61 155	0	33.5 85.1	0	66.75 169.6	Valgus	25	30	20	45	40	40	87	87	
11	N.D. 26+2 F	51 129.54	0	30 76.2	0	55.5 140.97	Varus	11	18	50	50	20	20	90	92	
12	I.K. 34+8 M	61.5 156.21	0	31 78.74	0	66 167.64	Straight	15	15	35	35	35	35	115	115	
13	N.M. 11+11 M	57.5 146.05	30	28.5 72.39	5	60 152.4	Valgus	8	8	82	82	35	35	100	100	

14	N.M. 27+1 F	59 149.86	0	32 81.28	0	62 157.48	Valgus	15	15	55	55	32	32	105	105	
15	R.K. 31+0 F	56.74 144.15	0	32 81.28	0	61 154.94	Varus	10	10	30	30	35	35	107	110	
16	J.K. 12+4 M	56 142.24	10	29.25 72.29	10	59 149.86	Valgus	12	12	25	35	30	30	105	105	
17	C.K. 16+3 F	60 152.4	7	31.5 79.38	0	61 154.94	R Valgus L Varus	12	15	60	38	32	30	107	123	
18	L.K. 18+4 F	59.5 151.13	1	31 78.74	0	64 162.56	Valgus	35	35	32	27	28	25	105	105	
19	R.K. 41+3 M	64.5 163.83	2	33 83.82	0	67 170.18	Varus	30	30	55	55	40	40	107	107	
20	R.K. 36+4 M	67 170.18	15	34 86.36	0	74 187.96	Varus	35	35	30	30	43	43	112	112	
21	T.P 5+6 F	34.5 87.63	0	23 58.42	5	40 101.6	Varus	35	35	35	35	25	25	107	107	
22	M.P. 7+9 F	45 114.3	2	26 66.04	20	47.5 120.65	Varus	25	25	30	30	34	34	110	110	
23	L.J. 34+9 F	59 149.86	0	34 86.36	25	61 154.94	R Varus L Straight	30	25	30	25	25	25	90	88	
24	K.M. 10+6 F	48.5 123.2	0	26 66	0	47.25 120	Valgus	26	26	65	65	45	45	140	135	Bilateral Valgus Hip Osteotomies
25	E.K. 6+7 M	41.75 106.05	0	22 55.88	0	45.5 115.57	Varus	12	12	35	35	40	40	110	110	
26	R.K. 2+4 M	33.5 85.09	5	20.5 52.07	25	33.75 85.73	Varus	15	15	4	40	45	45	123	123	
27	A.K. 7+7 F	42.75 108.59	0	25 63.5	7	46 116.84	Varus	10	10	40	40	30	30	110	110	
28	D.K. 2+6 F	31.5 80.01	0	18.75 47.63	0	32.5 82.55	Varus	10	10	30	30	35	35	122	122	
29	K.K. 0+9 F	24.75 62.87	0	17 43.15	25	26.5 67.31	Varus	15	15	65	65	40	40	125	127	
30	R.K. 6+2 M	46.25 117.48	45	25 63.5	25	47.23 120.02	Valgus	65	65	55	55	43	43	117	117	
31	S.K. 2+5 F	35 88.9	75	21.5 54.61	75	34.5 87.63	Varus	55	55	65	65	40	40	115	110	
32	R.J. 10+10 M	49.5 125.73	50	30 76.2	50	53 134.62	Varus	20	0	15	25	20	15	95	110	
33	B.C. 17+5 F	59 149.86	10	32.75 83.19	10	61 154.94	Varus	10	20	45	45	35	35	87	90	
34	F.C. 19+6 M	59 149.86	0	34 86.36	2	60.5 153.67	Valgus	10	10	42	42	35	30	80	90	
35	L.S. 17+3 M	62 157.5	0	37 94	65	67 170.2	Straight	45	37	25	37	50	50	130	146	Bilateral Valgus Hip Osteotomies Tibial Osteotomies
36	R.S. 17+8	59 150	0	31.5 80	0	59 150	Varus	30	45	30	30	30	42	105	105	Bilateral Valgus Hip Osteotomies
37	E.S. 15+8 M	59 150	0	32.5 82.6	0	62 157.5	R Valgus L Straight	25	30	45	50	45	45	100	105	Bilateral Valgus Hip Osteotomies
38	B.M. 12+8 M	54.5 138.43	2	28.5 72.39	1	56 142.24	Varus	10	10	45	45	35	35	102	102	
39	C.M. 12+1 F	49.5 125.73	0	26.25 67.31	0	51.5 130.81	Varus	15	15	50	50	30	30	105	105	
40	R.K. 6+4 M	41 104.14	0	23 58.42	0	43.5 110.49	Varus	10	0	30	40	22	22	100	100	
41	T.K. 2+7 M	34 86.36	5	20 50.8	5	34 86.36	Varus	15	15	40	40	32	32	125	124	
42	L.K.	31 78.745	6	17.5 44.45	5	30.5 77.47	Varus	15	15	40	40	30	30	123	123	

of height at skeletal maturity. A standard AP pelvis x-ray as well as AP x-rays of both knees were taken in all affected individuals. Protrusio acetabuli was diagnosed using Kohler's line. Evidence of iliac wing hypoplasia was subjectively judged by the senior author.

Results

All individuals presented in our study manifest characteristic features of MCDS. The pedigree supports an autosomal dominant inheritance pattern (Figure 3). Short stature is the main clinical presentation with a study average standing height of 145.6 cm and 156.9 cm in women and men, respectively. Overall average height for both males and females in skeletally mature MCD Schmid type is 151 cm (Table 2). The shortness of stature compared to the normal population is statistically significant ($p<0.001$). The average standing height of the 42 patients in this study is at the 5th percentile.

The difference in sitting height (Table 3) of the MCDS

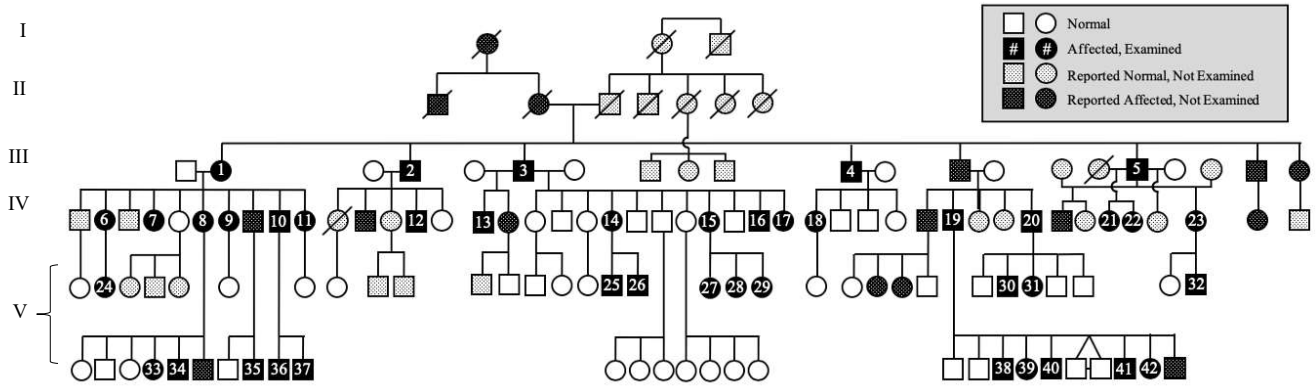

Figure 3. Pedigree representation of the MCDS cases within five generations of the study family. 135 members were investigated. 58 reportedly exhibited MCDS features, but only 42 participated in the study. Participants are numbered 1 through 42. Completely shaded shapes (n = 42; male = 21, female = 21) are affected individuals who were examined. Unshaded are those who were normal and examined (n = 50; male = 31, female = 15). Shaded shapes with white patterned dots represent individuals reportedly affected but not examined (n = 16; male = 9, female = 7). Unshaded shapes with black patterned dots represent individuals reported normal, but not examined (n = 27; male = 12, female = 15). A line through a shape (shaded or not) represents a deceased individual.

Table 2. Average standing height in skeletally mature participants with MCD - Schmidt Type (Age 16 and above) compared to normal average standing height in United States. The difference in standing height between MCD and normal population is statistically significant at $P < 0.001$.

	Number of Patients	Avg. Standing Height inch (cm)	Range inch (cm)	SD
MCD-Schmidt type: Female, age > 16	12	57.33 (145.63)	48.5 - 61.5 (123.2 - 156.21)	3.97 (10.1)
Unaffected: Female (US), age > 16		63.86 (162.2)		2.36 (6.0)
MCD-Schmidt type: Male, age > 16	11	61.77 (156.9)	59.0 - 67.0 (149.86 - 170.18)	2.68 (6.8)
Unaffected: Male (US), age >16		68.39 (173.7)		2.61 (6.64)
MCD-Schmid type: Female & Male, age > 16	23	59.46 (151.02)	48.5 - 67.0 (123.2 - 170.18)	4.04 (10.26)

Table 3. Average sitting height in skeletally mature participants with MCD-Schmid type (age 16 and above) compared to normal average sitting height in the United States. The difference in sitting height between MCD and unaffected population is statistically significant at $P < 0.001$.

	No.	Avg. Sitting Height inch (cm)	Range inch (cm)	SD
MCD-Schmidt type: Female, age > 16	12	31.6 (80.26)	26.5 - 34 (67.31 - 86.36)	1.92 (4.88)
Unaffected: Female (US), age > 16		33.82 (85.9)		1.3 (3.3)
MCD-Schmidt type: Male, age > 16	11	33.4 (84.84)	31 - 37 (78.74 - 94)	
Unaffected: Male (US), age >16		36.02 (91.5)		1.22 (3.1)
MCD-Schmid type: Female & Male, age > 16	23	32.44 (82.38)	26.5 - 37 (67.3 - 94)	1.96 (4.98)

patients compared to the normal population is also highly significant ($p<0.001$). The mean sitting height for the entire study group of patients is at the 9th percentile. In the skeletally mature group, the arm span is 7.25 cm longer than the standing height in females and 8.83 cm longer than the standing height in males, with the entire study group averaging a 6.48 cm difference in arm span and standing height (Tables 4 – 7). On average, 90% and 79% of MCDS patients in the study were below the 10th percentile in standing height and sitting height, respectively (Table 8)

Radiographically, all but seven study subjects demonstrated coxa vara with an average neck shaft angle of 105 degrees. Two additional individuals presented with

Table 4. Average sitting height as a percentage of average standing height of study participants.

	No.	Sit Ht x 100% / Stand Ht	Range	S.D.
Female, age > 16	12	55.15	52.1 - 58.8	2.21
Male, age > 16	11	54.06	50.4 - 59.7	2.89
Female & Male, age > 16	23	54.63	50.4 - 59.7	2.56
Female, age < 16	9	59.56	53.5 - 68.6	5.27
Male, age < 16	10	55.27	49.6 - 61.2	3.88
Female and male, age < 16	19	57.3	49.6 - 68.6	4.97
Entire series	42	55.84	49.6 - 68.6	4.02

Table 5. Average arm span in skeletally mature participants (age 16 and above) with MCDS.

	Number of Patients	Avg. Standing Height inch (cm)	nge inch (cm)	SD inch (cm)
MCD-Schmidt type: Female, age > 16	12	60.19 (152.88)	53 - 64 (134.6 - 162.56)	3.51 (8.92)
MCD-Schmidt type: Male, age > 16	11	65.25 (165.68)	59 - 72.5 (149.86 - 184.15)	4.93 (12.52)
MCD-Schmid type: Female & Male, age > 16	23	62.61 (159.03)	53 - 72.5 (134.6 - 184.15)	4.89 (12.42)

Table 6. Difference in length between arm span and standing height in study participants. (Normal = < 3.5 cm). On average, participants' arm span is greater than standing height, suggesting greater involvement in the lower extremities.

	No.	Avg arm span – standing height inches (cm)	Range inches (cm)	SD.
Female, age > 16	12	2.85 (7.25)	1 – 4.5 (2.54 – 11.43)	1.34 (3.41)
Male, age > 16	11	3.48 (8.83)	-0.5 – 8.0 (-1.27 – 20.32)	2.89 (7.33)
Female & Male, age > 16	23	3.14 (8.0)	-0.5 – 8.0 (-1.27 – 20.32)	2.19 (5.56)
Female, age < 16	9	1.64 (4.16)	-1.26 – 5.2 (-3.2 – 13.97)	2.03 (5.16)
Male, age < 16	10	2.1 (5.32)	0 – 3.75 (0 – 9.52)	1.26 (3.21)
Female and male, age < 16	19	1.88 (4.77)	-1.26 – 5.5 (-3.2 – 13.97)	1.66 (4.23)
Entire series	42	2.55 (6.48)	-1.26 – 8.0 (-3.2 – 20.32)	2.08 (5.28)

Table 7. Arm span to standing height ratio in study participants (Normal 1.00 - 1.03). With lower extremities affected more than upper extremities, the arm span to standing height ratio is increased to a value greater than the normal mean.

	No.	Arm Span/Standing Height Ratio	Range	S.D.
Female, age > 16	12	1.05	1.02 - 1.09	0.027
Male, age > 16	11	1.05	0.99 - 1.12	0.04
Female & Male, age > 16	23	1.05	0.99 - 1.10	0.035
Female, age < 16	9	1.04	0.97 - 1.16	0.06
Male, age < 16	10	1.04	1.00 - 1.09	0.03
Female and male, age < 16	19	1.04	0.97 - 1.16	0.04
Entire series	42	1.05	0.97 - 1.16	0.04

Table 8. Proportion of study participants whose standing height and sitting height is at or below 5th and 10th percentile.[25]

	No./Total	Percent
Participants with Standing Height at or Below 5th Percentile	26/42	62%
Participants with Standing Height at or Below 10th Percentile	38/42	90%
Participants with Siting Height at or Below 5th Percentile	23/42	55%
Participants with Sitting Height at or Below 10th Percentile	33/42	79%

neck shaft angles >120, but they had previously undergone valgus osteotomies. The normal femoral neck shaft angle is between 125-135 degrees, and varus is defined here as ≤120. Follow-up radiographs of the hips showed no evidence of premature osteoarthritis of the hips in this condition. In this study, 60% of patients exhibited iliac hypoplasia. No evidence of protrusio acetabuli was seen in any of the radiographs.

In studies on MCDS, knee alignment is reported to be in varus. In this series of 42 patients, approximately 50% of the patients demonstrated genu varum, approximately 33% demonstrated genu valgum, and approximately 10% of our population had straight knees.

Patients in this series exhibited normal life spans with no evidence of detectable intellectual deficits. No other congenital abnormalities of the musculoskeletal system were seen caudal to the knees in these patients.

Discussion

In this study, we describe the largest reported series of individuals of a single lineage who demonstrate features consistent with MCDS. Short stature and proximal femur involvement, specifically coxa vara, are defining characteristics of this condition.[23] Eighty-three percent of the patients in our study exhibited these two main clinical features. Autosomal dominant inheritance of MCDS with no skipped generations was noted for the 42 affected members in this large single lineage study. The mean standing height of MCDS females and males in our study was 145 cm and 156 cm, respectively. In comparison, the mean height of normal U.S. females and males is 162 cm and 172 cm, respectively. These results are both statistically significant compared to the normal population ($p < 0.001$) and consistent with Schmid's original sample describing overall average standing height for MCDS individuals as 150 cm. In addition, our findings confirm that the short stature is due to dysplasia of the lower extremities rather than that of the axial skeleton, with an average sitting to standing height ratio of 0.55, approximately two standard deviations higher than normal individuals.[24] Moreover, our findings agree with previous reports in the literature of minimal skull, spine, or trunk involvement.[6]

Our study confirms previous radiological findings related to proximal femur deformity with 83% of our patients presenting with coxa vara and an average neck shaft angle of 105 degrees. All study subjects declined elective surgery to correct bony alignment, gait deformity, and muscular insufficiency. This is likely because the study population is from a single lineage with individuals who are aware of the natural progression of MCDS in their family. Remarkably, despite this deformity, the vast majority of our study population remained clinically functional with very little limitation of activities. Premature osteoarthritis of the hips was not a notable feature in our study population, and only one patient in his 60s showed evidence of osteoarthritis. Most of the study population, however, did exhibit waddling gait due to weakness of the gluteus medius in the setting of coxa vara.

Due to the breadth of our patient population, we were able to elucidate more patterns associated with MCDS. Previous accounts described predominantly genu varum presentations estimating greater than 60% of patients with MCDS have genu varum.[2] However, while our study population consistently demonstrated coxa vara deformity proximally, variance in deformity occurred distally at the knee. Of the 42 patients, only 50% demonstrated genu varum, notably less than estimates in current literature. Approximately 33% of the study population demonstrated genu valgum and 10% had straight knees. Our results suggest that diversity of deformity can occur at the knee joint and must be considered by the orthopaedic community in diagnosing and treating MCDS.

Conclusion

This is the largest reported series of a single lineage MCDS. Autosomal dominant mode of inheritance is confirmed in our pedigree. Subischial involvement in the lower extremities predominates compared to involvement of the trunk or spine. The skull and upper extremities are relatively normal in these patients. Coxa vara is a consistent finding occurring in the majority of our patients, but this confers minimal lifestyle disability with no evidence for premature osteoarthritis of the hips. The previously established knee deformity in this condition is varus, but our series revealed a third of patients with valgus knees. The long-term follow-up reveals that these patients exhibit a normal life span in the setting of these findings.

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