Skeletal Radiology
Journal of the International Skeletal Society A Journal of Radiology, Pathology and Orthopedics

10.1007/s00256-005-0939-2

Case Report

Familial short fifth metacarpals and insulin resistance

Muwafag Hyari[1], Hanan Hamamy[1], Muries Barham[1], Azmy Al-Hadidy[2] and Kamel Ajlouni[1]

(1) National Center for Diabetes, Endocrinology and Genetics, P.O. Box 13165, 11942 Amman, Jordan

(2) Department of Radiology, Jordan University Hospital, Amman, Jordan

Kamel Ajlouni
Email: hananhamamy@yahoo.com
Phone: 962-6-5353374
Fax: +962-6-5353376

Received: 14 February 2005 **Revised:** 25 March 2005 **Accepted:** 31 March 2005

Abstract Very few reports on the phenotype of short fifth metacarpals have been published in the medical literature. We report a Jordanian family in which three sisters aged 15, 13 and 8 years revealed bilateral shortening of the fifth fingers and radiological shortening of the fifth metacarpals. The father had unilateral short fifth metacarpal. The elder two sisters, their father as well as their brother and another sister manifested insulin resistance. Spherocytosis was diagnosed in one of the girls and her father. The parents are non-consanguineous. This constellation of findings has not been previously reported and could point to the presence of two disorders segregating in the family or to a novel syndrome with autosomal dominant inheritance and variable expressivity.

Keywords Short fifth metacarpals - Spherocytosis - Insulin resistance - Radiographs

Introduction

Few reports have been published describing the phenotype of short fifth metacarpals, without the presence of short fourth metacarpals. Patel et al. described an extended family with three members having insulin resistance and short fifth metacarpals [1]. Another single case of idiopathic isolated bilaterally symmetrical brachymetacarpia of the fifth finger was reported in a woman aged 32 years [2]. Brachymetacarpia V evaluated by measuring the length of the fifth metacarpals showed a higher frequency among 25

children with familial short stature than among 23 controls [3]. A single report associating short fifth fingers with spherocytosis was published in Russian [4].

The family reported here showed a constellation of three findings in more than one member of the family. These findings included short fifth metacarpals, insulin resistance and spherocytosis. According to the parents, no other family members have these features.

Short fifth metacarpal is defined as a gap of 2 mm or more between the distal end of the fifth metacarpal bone and a tangential line connecting the distal ends of the third and fourth metacarpals [5]. Insulin resistance is defined as a clinical state in which a normal or elevated insulin level produces an attenuated biological response and is observed years before the onset of clinical hyperglycemia and the diagnosis of type 2 diabetes [6]. The insulin resistance in several syndromic forms of extreme insulin resistance such as type A, Rabson-Mendenhall and leprechaunism syndromes has been shown to be caused by mutations in the receptor gene [7]. Insulin resistance was evaluated according to the HOMA method (basal homeostasis model assessment), where it is calculated by the equation: [glucose (mmol) × insulin level (IU/ml)]/22.5, and the normal value is estimated at less than 1.1. Insulin resistance would be diagnosed if the value exceeds 1.1 [8].

Spherocytosis was diagnosed through blood film interpretation and the standard osmotic fragility test (this test measures the level of hemolysis of red cells placed in a gradient series of hypotonic solutions (4.6 5.9 g NaCl/l). High levels of osmotic fragility usually point to the presence of spherocytosis.

Case report

The proband was a girl aged 11 years (case II-3), who presented to the endocrine clinic with the main complaint of short stature. At that time, her height was 136 cm (5th percentile). She was followed up at the clinic and continued to gain height reaching 152 cm at the age of 13 years (10th percentile). Past history revealed that following an episode of abdominal pain at the age of 3 years, she was diagnosed by hematologic, bilirubin level and osmotic fragility testing to have congenital spherocytosis with splenomegaly. Osmotic fragility testing for spherocytosis in her parents at that time showed that her father had spherocytosis. During the follow-up of the proband in the endocrine clinic, she was diagnosed to have bilateral short fifth fingers and bilateral short fifth metacarpals on radiographs. The proband also showed insulin resistance by the HOMA method. Her parents and all her siblings were recruited and assessed for short fifth metacarpals on radiographs, for insulin resistance and for spherocytosis.

The parents are not consanguineous. The father has insulin resistance, short fifth metacarpal in the right hand and spherocytosis. Two sisters aged 15 and 8 years manifested bilateral short fifth metacarpals, and the elder sister showed insulin resistance. Their brother and another sister aged 12 years showed insulin resistance. The mother was

free from all three findings. The results for parents and all offspring are presented in Table 1. There was no dysmorphism and no history of developmental problems. Renal and thyroid function tests, and general blood biochemistry showed no abnormality. No family members were hypertensive or diabetic; the father and eldest son were overweight.

Table 1 Clinical features of parents and all offspring

	Brother (II-1)	Sister (II-2)	Proband (II-3)	Sister (II 4)	Sister (II-5)	Father (I-1)	Mother (I-2)
Age (years)	17	15.5	13.5	12.5	8	58	42
Height (cm)	173	158	152	154	125	169	164
Weight (kg)	78	47	41	45	30	79	68
Short fifth metacarpal[s]	No	Bilateral	Bilateral	No	Bilateral	Right	No
Acne	No	Yes	No	Yes	No	No	No
Hirsutism	NA	No	No	No	No	NA	No
Fasting insulin (normal = 5 25 IU/ml)	12	14	11.8	10.8	4.9	13.2	4.7
Fasting blood sugar (mg/dl)	80	80	69	83	89	109	67
Hb (g/dl)	17	10.4	10.3	14.2	12.4	15.9	13.9
HOMA (normal = less than 1.1)	2.37	2.77	2.01	2.21	1.08	3.55	0.78

[a]Measured as the distance between distal end of the fifth metacarpal bone and a tangential line connecting the distal ends of the third and fourth metacarpals (normal = less than 2 mm)

The family pedigree is presented in Fig. 1, and the phenotype and radiological images of the hands are shown in Fig. 2 and Fig. 3.

Fig. 1 Family pedigree

Fig. 2 Short fifth fingers in the proband (II-3) and her sister (II-5)

Fig. 3A D Hand radiographs showing bilateral short fifth metacarpals in the proband (case II-3), her sisters (II-3, II-5) and their father (I-1)

Discussion

Short fifth metacarpals have only been reported in a few cases in the literature [*1*, *2*], while short fourth metacarpals are known to be associated with distinct syndromes such as pseudohypoparathyroidism and Turner syndrome. The three sisters with bilateral short fifth metacarpals (cases II-2, II-3, II-5) in this family showed normal levels of calcium and phosphate in blood, and were of normal intelligence. Their bone age was compatible with the chronological age. Furthermore they did not show the familial short stature reported to be associated with short fifth metacarpal [*3*]. The proband, although presenting with short stature at the endocrine clinic when 11 years old, showed an increase in height of 16 cm over the following 2 years.

There is only one report in the literature describing three members of an extended family having both insulin resistance and the phenotype of short fifth metacarpals [*1*]. Our report describes a second family with these two features, where insulin resistance and unilateral short fifth metacarpal were seen in the father, and insulin resistance with bilateral short fifth metacarpals were evident in two of his daughters (cases II-2,II-3). The brother (II-1) and another sister (II-4) showed only insulin resistance, while the youngest sister (II-5) manifested bilateral short fifth metacarpals but not insulin resistance. She is only 8 years old and should be assessed again around puberty for insulin resistance. The father is also known to have spherocytosis.

In the Arab world, the prevalence of the metabolic syndrome was 17% among Palestinians in the West Bank and 21% among Omanis, using the WHO and ATPIII criteria respectively [*9*, *10*]. Among American Arabs, the age-adjusted prevalence of the metabolic syndrome was 28% and 23%, using the WHO and ATPIII criteria respectively [*11*]. To our knowledge, no large-scale study associating short fifth metacarpal with the metabolic syndrome has been done; a positive association, if proved, could predict an individual  s risk of developing type 2 diabetes in the future.

The sole report (from Russia) associating short fifth finger with spherocytosis [*4*] prompted us to investigate all members of the family for this disorder using the osmotic fragility test. The proband (case II-3) and her father had an abnormal reading for the osmotic fragility test (Table 1), pointing to the diagnosis of congenital spherocytosis. It could be that the spherocytosis in this family is unrelated to the short fifth metacarpals, although a relationship cannot be disregarded.

This constellation of findings has not been previously reported and could point to the presence of two disorders segregating in the family or to a novel syndrome with autosomal dominant inheritance and variable expressivity.

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