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Metacarpal 4–5 Fusion with X-linked Recessive Inheritance

LEWIS B. HOLMES,[1] ERNST WOLF,[2] AND OLLI S. MIETTINEN[3]

INTRODUCTION

Hereditary hand malformations typically have an autosomal dominant mode of inheritance [1]. The only exception known to us is fusion of metacarpals 4 and 5, which Orel [2] described in 1928 in a family with a pedigree pattern suggesting X-linked recessive inheritance. The present report corroborates Orel's finding by describing a fusion of metacarpals 4 and 5 in a pedigree which also indicates X-linked recessive inheritance. It is shown that the gene locus for metacarpal 4–5 fusion is unlikely to be closely linked with that of protanomalous color deficiency.

SUBJECTS AND METHODS

The propositus was a man in whom a deformity of both fifth fingers was noted during hospitalization for treatment of a duodenal ulcer. He reported that this deformity, which the family calls a "bum" finger, has occurred in several male members of his family. His history was supplemented by separate interviews with several other members of the family. These interviews revealed 10 affected individuals in addition to the propositus, all of them males (fig. 1).

Eight of the 11 affected males were available for examination, and all of them clearly had deformities involving one or both of their fifth fingers. In addition, four males (IV-22, IV-27, IV-28, and V-15) and five females (III-20, IV-9, IV-21, IV-24, and V-28) reported not to have the anomaly were studied and found to have normal metacarpals, clinically and roentgenographically, with normal dermatoglyphics. These negative findings have added value in that three of the normal males were offspring of either potential or proven carrier mothers, and three of the females were proven carriers.

The color vision of these family members (fig. 1) was tested using the anomaloscope, the Farnsworth D-15 test, the Ishihara test, and the Hardy-Rand-Rittler pseudoisochromatic plates [3].

As an additional marker for linkage evaluation, the presence or absence of the Xg antigen on red blood cells was determined, but all family members tested were Xg^a positive. Glucose-6-phosphate dehydrogenase activity was determined by the method of

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[1] Genetics Unit, Children's Service, Massachusetts General Hospital, and the Department of Pediatrics, Harvard Medical School, Boston, Massachusetts 02114.

[2] Retina Service Laboratory of the Massachusetts Eye and Ear Infirmary, and the Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts 02114.

[3] Department of Epidemiology and Biostatistics, Harvard School of Public Health, Boston, Massachusetts 02115.

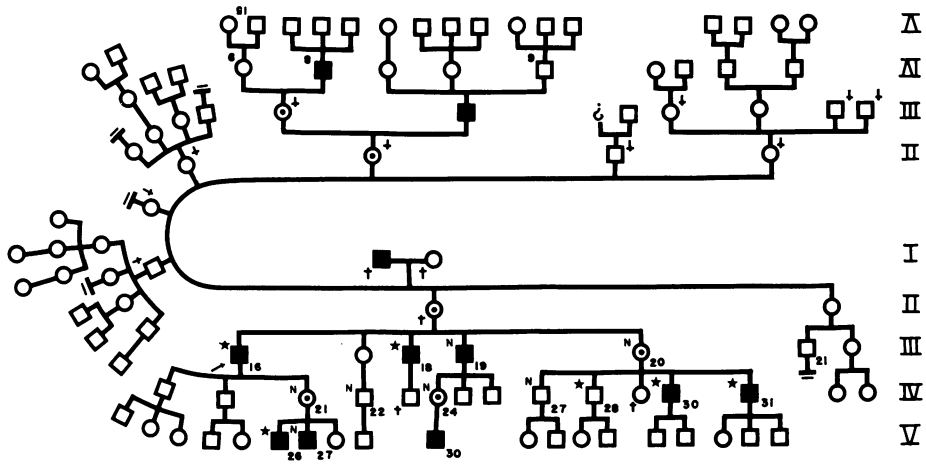

FIG. 1.—Pedigree. Solid square = affected males; dotted circle = carrier females. Star denotes protanomalous color deficiency; *N* denotes normal color vision; cross denotes deceased individuals. Arrow indicates propositus.

Beck [4] on red blood cells from individuals IV-24 and IV-30; both had normal levels of activity. Chromosome analysis on white blood cells of one individual (IV-8) showed a normal 46,XY karyotype using the routine Giemsa method (*p*H 6.8) of staining.

RESULTS

Clinical Characteristics

Among the eight affected males examined, metacarpal 4–5 fusion was bilateral in six and unilateral in two. The clinical signs included lateral deviation of the fifth finger (fig. 2*a*), shortness of metacarpals 4 and 5, excessive separation between their distal ends (fig. 3*a*), and inability to bring an affected fifth finger in parallel to the fourth finger. There was no abnormality of flexion of the affected fingers.

Radiographs of the hands showed varying abnormalities in metacarpals 4 and 5. In the extreme there was complete fusion, with the proximal phalanx of the fifth finger resting on the lateral and distal part of a single wide metacarpal (fig. 2*b*). In other instances there was fusion of the proximal one-half to two-thirds of the fourth and fifth metacarpals associated with separation of the distal epiphyses (figs. 3*b*, 4). The unilaterality of the anomaly in two individuals was corroborated by the roentgenograms (fig. 4).

None of the persons examined had any other anomalies of the hands or feet. In particular, roentgenograms of the feet of eight affected males and three carrier females showed no abnormalities.

Dermatoglyphics showed two abnormalities. First, triradii *c* and *d*, normally located at the base of the fourth and fifth fingers, were absent in three of the eight men (table 1). In these instances the metacarpal abnormality was relatively severe. In an additional case there was a single triradius in place of triradii *c* and *d*. In general, the more severe the metacarpal abnormality, the more likely an absence

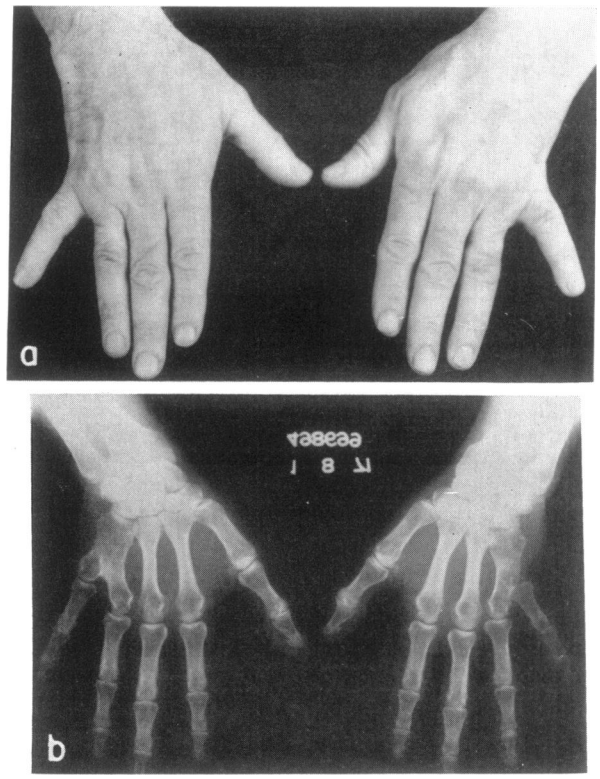

FIG. 2.—Hands of the propositus (III-18) showing laterally deviated fifth fingers and fused metacarpals 4 and 5 with the proximal phalanx of the fifth fingers resting on the lateral aspect of this fused bone.

of triradii *c* or *d*. The second abnormality of the dermatoglyphics was a slight increase in the atd angles: in the five examined individuals with a *d* triradius, the mean values were 51.5° and 56.7° for the left and right hands—in contrast to the mean value of 48° in the general population of England [5].

Mode of Inheritance

The pedigree (fig. 1) is strongly indicative of X-linked recessive inheritance: all affected males are related through maternal relatives, there are three instances of affected grandfathers and grandsons, and there is no male-to-male transmission.

Linkage with Colorblindness

Possible linkage between the loci of metacarpal 4–5 fusion and protanomalous colorblindness was evaluated by considering the descendants of II-7. The available information is given in figure 1.

The recombination fraction was estimated by the likelihood ratio ("backward odds") method of Haldane and Smith [6]. The likelihood ratio function is de-

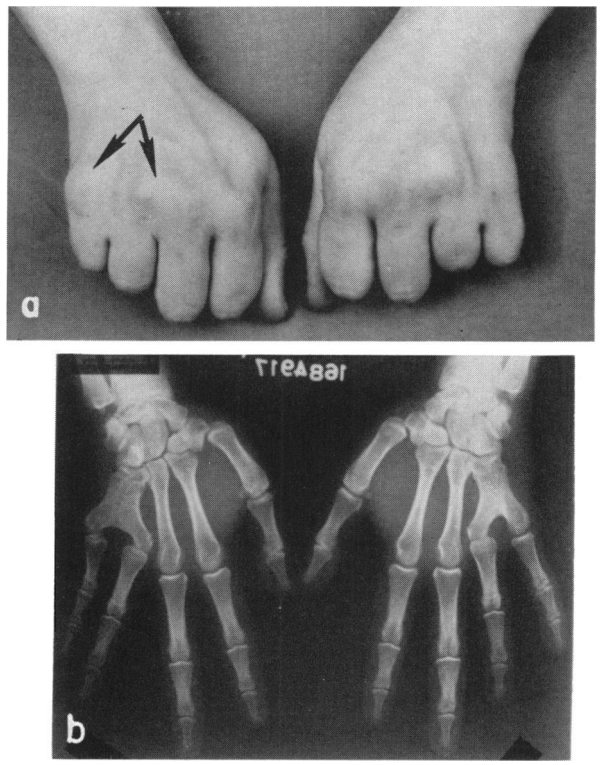

FIG. 3.—Hands of the grandson (V-26) of the propositus showing in his fist the closeness of knuckles 3 and 4 and the wide separation of 4 and 5 (arrows). The X-ray shows distal forking of the fused metacarpals 4 and 5 with lateral deviation of the right ring finger as well as the fifth.

picted in figure 5. It gives no suggestion of linkage, since the maximum of the function corresponds to $\theta = .5$. Moreover, the curve is inconsistent with close linkage: the lower bound of an approximate two-sided 90% confidence interval for θ is .26, computed according to Bode and Miettinen [7].

DISCUSSION

Similar fusion of metacarpals 4 and 5 has been reported by Lerch [8], Habighorst and Albers [9], and Shiryak [10]. The first two reports indicated additional affected family members. However, the mode of inheritance in these families is inconsistent with X-linked recessive inheritance in that there was male-to-male transmission and affected females were present.

The Russian boy reported by Shiryak [10] is of particular interest because of his possible relationship to the family we have studied. The first affected member of the family presented here was born of Jewish parents in Vilna, Latvia, in the middle of the nineteenth century. He emigrated to the United States and adopted the family name of Cohen.

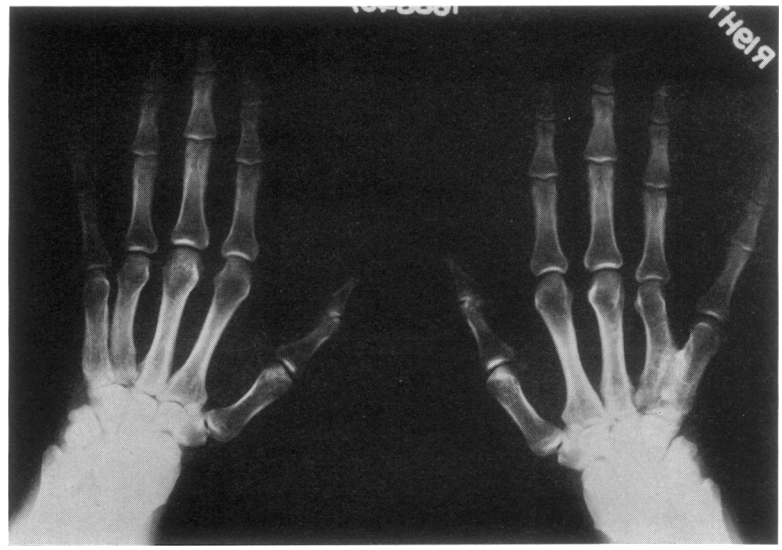

FIG. 4.—X-ray of IV-30 showing of metacarpals 4 and 5 in the right hand and little, if any, changes in the left hand.

TABLE 1

DERMATOGLYPHICS IN EIGHT MALES AND THREE CARRIER FEMALES OF METACARPAL 4–5 FUSION

SUBJECT	DEGREE* OF METACARPAL 4–5 FUSION		PRESENCE† OF TRIRADII				atd ANGLE		PRESENCE† OF HYPOTHENAR PATTERN	
			Left		Right					
	Left	Right	*c*	*d*	*c*	*d*	Left	Right	Left	Right
Affected males:										
III-16	2	1	—	—	—	—	?	?	—	+
III-18	2	2	+‡		+‡		(43)§	(60)§	—	+
III-19	2	1	—	—	+	+	?	60	+	+
IV-8	1	1	—	—	+	+	?	58	—	—
IV-30	0	1	+	+	+	+	44	48	—	—
IV-31	0	1	+	+	+	+	60	70	—	+
V-26	1	1	+	+	+	+	52	47	—	—
V-27	1	0	+	+	+	+	50	57	—	+
Average	...	...	...		...		51.5	56.7	...	...
Carrier females:										
III-20	0	0	+	+	+	+	37	36	—	+
IV-21	0	0	+	+	+	+	65	62	—	—
IV-24	0	0	+	+	+	+	40	59	—	—

NOTE.—There is a rough correlation between the degree of metacarpal fusion and the absence of triradii *c* and *d*.

* Degree: 2 = single bone in place of two; 1 = fusion 1/2 to 2/3 of length; 0 = minimal or no fusion.

† Presence: + = present; — = absent.

‡ Intermediate position of a single triradius for *c* and *d*.

§ These angles excluded from calculation of averages.

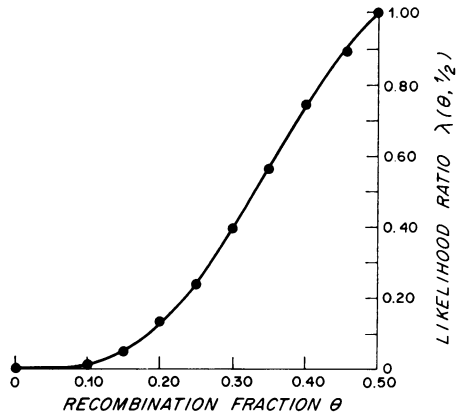

FIG. 5.—Likelihood ratio function for protan and metacarpal 4–5 fusion, showing no evidence of linkage.

The absence of triradii *c* and *d* in some of the affected men presumably is a reflection of the same morphologic abnormality that caused the adjacent metacarpal anomaly. In this respect it is analogous to type II syndactyly, a localized developmental anomaly associated with an absence of triradii *b* and *c* [11].

Inasmuch as it appears from the present data that the gene locus of metacarpal 4–5 fusion with X-linked recessive inheritance is not close to that of protanomalous colorblindness, there could be close linkage with the Xg locus. Unfortunately, the family presented here is not informative about the latter possibility.

SUMMARY

A family with 11 cases of metacarpal 4–5 fusion is reported. The clinical features are presented, the mode of inheritance is inferred to be X-linked recessive, and the recombination rate of the gene with that of protanomalous colorblindness is estimated to be high.

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