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IDENTICAL TWINS DISCORDANT FOR CONGENITAL SPINAL ANOMALIES

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SUMMARY

A twin pair, discordant for congenital spinal cervical anomalies, is described. Zygosity chances are calculated on the basis of initial dizygosity chance, sex likeness, red cell antigens, serum types, red cell enzymes, and dermatoglyphic data. The chance for monozygosity adds up to 0.9992. Literature data on cervical anomalies in twins are reviewed.

It is concluded that, although the inheritance of spinal anomalies, such as hemivertebra, is still an open question, this twin pair supports the present trend of ideas that most of these anomalies are caused by peripheral, nongenetic factors.

The purpose of this paper is to describe congenital spinal anomalies present in only one of two MZ twin sisters and to search for the possible factors which might account for this discordant, erroneous development of the spine.

CASE REPORTS

The twin girls Veerle and Véronique B. were born after a full-term uneventful pregnancy, when maternal and paternal age was respectively 30 and 29 years. It was the mother's third pregnancy. There was no history of previous miscarriages or stillbirths. The delivery was easy without the use of forceps or vacuum extractor. There was one dichorionic and diamniotic placenta. (Microscopic examination of the dividing membrane was performed by Dr. Derom, Ghent.) Veerle, born first in vertix presentation, had a remarkably short umbilical cord, weighed 2.70 kg and was 49 cm long. Véronique, born ten minutes later in breech position, weighed 2.75 kg and was 47 cm long.

The twins developed normally. They were simultaneously affected by the common child diseases such as measles, chickenpox, and rubella. They both started to walk without aid at 13 months, began to speak at 12 months, and got their first teeth at 8 months. Enuresis nocturna stopped in both of them at the age of 3 years.

At the time of the first examination the twins were 4.4 years old. Veerle's height was 108 cm and her weight 18 kg; Véronique was 111 cm long and weighed 19 kg.

The following physical characters were strikingly identical: colour, form, thickness, and implantation of the hair; length, thickness, and implantation of eyelashes and eyebrows; form of the face; colour of the skin; colour and repartition of the freckles; form of the nose;

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thickness of the lips; mass of the tongue; and colour and structure of the eyes. The form and structure of the lobulations of the external ear were mirror images in both twins. Veerle was left-handed and Véronique right-handed.

Characterwise Veerle seemed to be more sly, firm and boylike, and more alert than Véronique who was more sensible and careful.

Besides the numerous points of resemblance, there were some striking differences. Indeed, Veerle presented the following features:

— a shorter neck with head tilting to the right in frontal plane and to the left in horizontal plane;

— a slight cervico-dorsal scoliosis with convexity to the right; neck movements, normal in the antero-posterior direction, but laterally limited 40° from the midline on the right, 20° on the left;

— slight tilting of the right shoulder (1 cm);

— a slight dorsal rib hump (5 mm) on the left;

— deviation of the occipital axis to the right over 5 mm.

Roentgen studies showed cervico-dorsal scoliosis with convexity to the right, posterior spina bifida of C6, right hemivertebra of Th2 with unilateral rib (twelve ribs on the right and eleven on the left), and lumbarization of S1. Tomography revealed assimilation of posterior arc and right lateral (massive) part of the atlas. The left part slightly hypotrophic could be individualized. None of these anomalies were present in Véronique.

Family Data

There was no indication for familial congenital malformations, as torticollis or short neck. In the paternal family there were two cases of twins.

The *orthopedic and roentgen examination* of the mother (33 years), father (34 years), sister (7 years), and brother (6 years), did not reveal any anomalies, not even in a frust condition.

The *blood examinations* were performed in Dr. Derom's (Ghent)[1] and Dr. Robson's (London) laboratory. The results are seen in Table I. Besides the red cell antigens, the serum types and red cell enzymes were determined in order to have as many data as possible for the zygosity calculation. The first examinations had shown indeed a great similarity amongst all the family members.

Dermatoglyphic Data

Digital and palmar dermatoglyphics of both twins were very similar (Tables II and III).

The total finger ridge count (TFRC) was 55 in Veerle and 50 in Véronique, thus showing a difference of only 5 (Table II).

The digital patterns (Table II) were identical on all fingers in both twins, except on the second digit of the right hand, where Veerle presented an arch and Véronique an ulnar loop. They both showed several arches (Veerle on four fingers and Véronique on three), which is a rather rare pattern in the general population.

The palmar patterns were similar in the four hands. Moreover, striking resemblances between both right hands and between both left hands were found:

— Radial loops were present in the hypothenar regions of the four hands.

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TABLE I
BLOOD MARKERS

	Veerle	Véronique	Father	Mother	Brother	Sister
Red cell antigens:						
ABO	O	O	O	O	O	O
Rhesus phenotype	CCDee	CCDee	CcDee	CCDee	CCDee	CCDee
Probable genotype	CDe/CDe	CDe/CDe	CDe/cde	CDe/CDe	CDe/CDe	CDe/CDe
Cw	—	—	—	—	—	—
MNSs	MMSs	MMSs	MMSS	MNss	MNSs	MNSs
Duffy (Fy^a)	—	—	—	—	—	—
Kell (K)	—	—	—	—	—	—
P	—	—	—	+	—	—
Serum types:						
Haptoglobulins (Hp)	2-1	2-1	2-1	2-1	2-1	2-1
Group specific component (Gc)	2-1	2-1		2-1		
Transferrine (Tf)	C	C	C	C	C	C
Red cell enzymes:						
Acid phosphatase (AcP)	BA	BA	BA	BA	A	BA
Phosphoglucomutase (PGM)	2	2	2-1	2-1	1	2-1
Adenylatekinase (AK)			1	1		
Peptidase A			1	1		
Peptidase B			1	1		
Peptidase C			1	1		
Peptidase D			1	1		
Adenosinedeaminase (ADA)	1	1	1	2-1	1	2-1
Diaphorase	1	1	1	1	1	1

TABLE II
DIGITAL DERMATOGLYPHICS

	TFRC	Left fingers				
		1	2	3	4	5
Veerle	55	UL (7)	A (0)	A (0)	UL (5)	UL (12)
Véronique	50	UL (8)	A (0)	A (0)	UL (11)	UL (9)
		Right fingers				
		1	2	3	4	5
Veerle		UL (12)	A (0)	A (0)	UL (10)	UL (9)
Véronique		UL (5)	UL (4)	A (0)	UL (8)	UL (5)

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TABLE III
PALMAR DERMATOGLYPHICS

		Max *atd* angle	*ab* ridge count	*bc* ridge count	*cd* ridge count
Veerle	left	32	34	19	33
	right	32	31	17	35
	left + right	64	65	36	68
Véronique	left	37	34	24	33
	right	36	35	23	29
	left + right	73	69	47	62

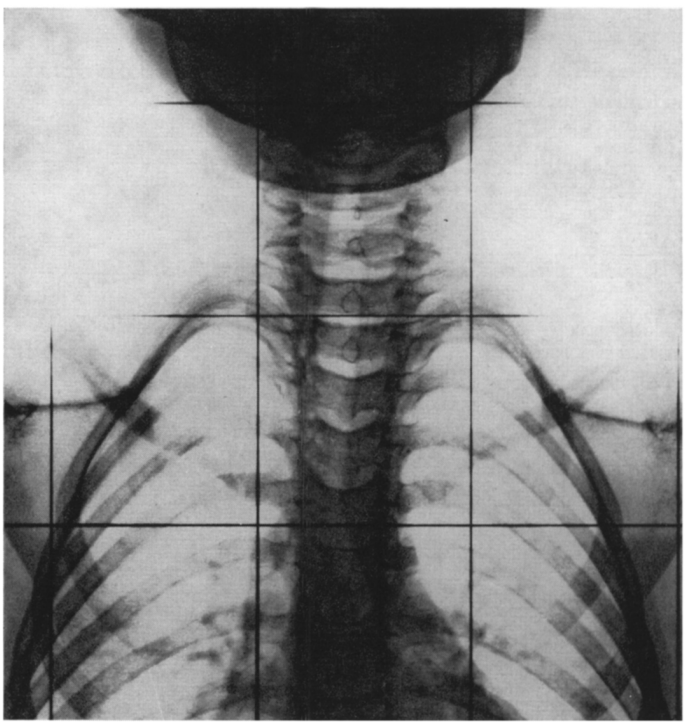

FIG. 1. *Twin Véronique: normal cervico-dorsal spine.*

— The main lines A, B, and D had the same general course on the four palms; the main-line index on both left hands was 14, on both right hands 16.

— Line C formed a loop on both right hands in the fourth interdigital area and on both left hands in the third interdigital area.

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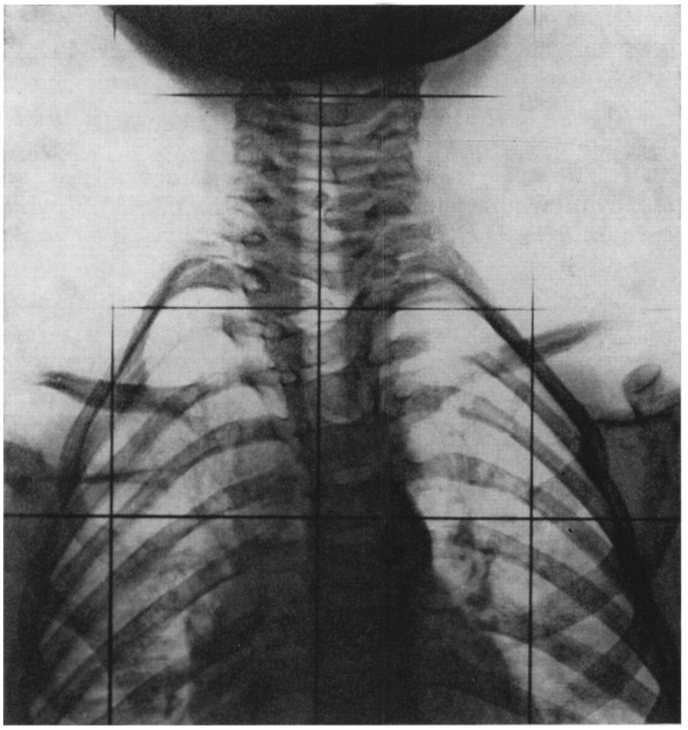

FIG. 2. *Twin Veerle: cervico-dorsal scoliosis, spina bifida of* C6, *right hemivertebra* Th2.

— The quantitative palmar data such as maximal *atd* angle, *ab*, *bc*, and *cd* ridge counts, are shown in Table III. The difference between the *atd* angles of both twins was 9. Although the palms were very similar, they were not identical.

DISCUSSION

Zygosity

The chance for monozygosity was calculated according to Maynard-Smith et al. (1961). The following factors were taken into account: initial dizygosity chance, sex likeness, blood analysis, and quantitative dermatoglyphic data. It has to be kept in mind that the qualitative dermatoglyphic data, such as the digital and palmar patterns, although indicating the similarity and monozygosity of both twins, cannot be used for statistic studies; moreover that their configuration is both genetically and environmentally determined. According to Maynard-Smith et al. (1961), the probability to be dizygotic for a like-sexed twin pair with a TFRC intrapair difference of 5 is 0.23 and with an *atd* angle intrapair difference of 9 is 0.80.

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As can be seen from Table IV, the relative chance for dizygosity:monozygosity was 0.0008385:1, so that the probability that the twins were MZ was

$$\frac{1}{1 + 0.0008385} = 0.9992$$

This calculation definitely proved that the twins were MZ, which had already initially been suspected from their external appearance.

TABLE IV
RELATIVE CHANCE FOR DIZYGOSITY

Estimated initial dizygosity chance			2.3333
Sex likeness			0.5
Red cell antigens:	ABO		1
	Rhesus		0.5
	MNSs		0.5
	P		0.5
	Kell		1
	Duffy		1
Serum types:	Hp		0.5
	Tf		1
Red cell enzymes:	AcP		0.5
	PGM		0.25
	AK		1
	Peptidase	A	1
		B	1
		C	1
		D	1
	ADA		0.5
	Dia		1
Difference in ridge count			0.23
Difference in *atd* angle			0.80
			0.0008385

Chance for dizygosity $= \frac{0.0008385}{1.0008385} = 0.0008$

Chance for monozygosity $= 1 - 0.0008 = 0.9992$

The twins had a dichorionic, diamniotic placenta. Although this is no argument in favour of monozygosity, it does not exclude it. Indeed, when the cleavage of the zygote occurs very early, at 2-3 days after fertilization, MZ twins have a dichorionic placenta, which is the case in about 30% of all MZ twin births.

Discordance

Malformations occur much more in MZ than in DZ twins and are more frequently concordant in MZ than in DZ twins. The observation of discordant congenital anomalies in MZ twins can be useful in the study of the interaction of environmental and hereditary factors in development, on condition that zygosity is accurately known.

Discordant inheritance among MZ twins can theoretically be ascribed to:

(1) unequal segregation of cytoplasmic material capable of transmitting the abnormality;

(2) effect of teratologic influences, acting after cleavage in only one of the twins: in the case of hemivertebra, these factors should act from the fourth week to the fourth month of gestation, when the vertebrae are in a critical developmental phase. As teratologic mechanisms can be envisaged: somatic mutations, chromosomal errors, circulatory or nutritional disturbances, enzyme inhibitions, endocrine disturbances, mechanical factors, infections, immunologic phenomena, etc.

In view of the fact that the anomalies were restricted to a localized region and that the child was mentally normal and alert, autosomal abnormalities can be excluded. The other factors cannot be proven nor excluded.

The literature provides reports as well of *concordant* as of *discordant* occurrence of hemivertebra in MZ twins.

Haffner (1936) described concordant identical twins with scoliosis and spinal deformities, such as lumbar hemivertebrae. He concluded that the formation of hemispondilus must be due to the considerable independence concerning segmentation of the two halves of the spine and that the teratogenic period must lie between the second and the fourth week of fetal life. He furthermore concluded that these concordant malformations indicated that the disposition to the formation of hemispondilus was hereditary.

Gedda and Iannaccone (1959) observed the concordant occurrence in MZ twins of cervico-occipital anomalies, such as torticollis of the schisosynostotic type, however with a different degree of expressivity.

Degenhart (1964) described a set of triplets of which two, including the proband, were MZ twins. The proband presented hemivertebra of Th4, unilateral absence of a rib, scoliosis, spina bifida of S1, and heredodegenerative nystagmus and cataracts. The cotwin presented spina bifida of S1. The third triplet had spina bifida of S1 and S2, but the rest of the spinal column was normal. The father of the triplets had spina bifida of S2. A sister of the father had given birth to a stillbirth with " open back ". The MZ twins were obviously discordant for hemivertebra, the occurrence of the spina bifida being a separate familial condition. It is moreover known that spina bifida occulta S1-S2 is extremely frequent in the general population.

H.A. and L.F. Peterson (1967) reported discordant MZ twins: the shorter twin had multiple hemivertebra and the other had a normal spinal column. The authors suggested that, at least in that set of twins, the congenital hemivertebrae were not genetically determined.

Genetics

Familial occurrence of vertebral anomalies has often been reported (Degenhart 1964). However, the anomalies present are very complex, differ in type and localization, and show a high degree of variability and different expressivity. Furthermore, because of the lack of sufficient systematic roentgenologic evaluations of " normal " family members of patients with vertebral anomalies, a possible pattern of familial occurrence of hemivertebra with associated anomalies is not yet established.

In view of this fact and of the disparate twin data, the possible inheritance of hemivertebra is as yet an unsolved problem.

CONCLUSIONS

1. This twin pair once more shows that MZ twins are not necessarily identical. It has to be kept in mind that genetic alterations, developmental accidents, and environmental uterine influences can affect the development of one of the twins in such a way that it differs considerably at birth from its cotwin.

2. Twin studies are only valuable in the appraisal of the etiologic factors of a congenital disease when zygosity is accurately determined. This may necessitate analysis of plasmatic and enzymatic blood data.

3. The inheritance of spinal anomalies, *in casu* hemivertebra, remains an open question. Our twin pair supports the present trend of ideas that the majority of these anomalies is caused by peripheral, nongenetic factors.

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RIASSUNTO

Viene descritta una coppia di gemelle discordanti per delle anomalie della colonna a livello cervicale. La probabilità di monozigotismo — calcolata in base alla probabilità iniziale di dizigotismo, del sesso, dei gruppi sanguigni, delle proteine plasmatiche, degli enzimi eritrocitari e dei dermatoglifi — risulta di 0.9992. Vengono passati in rassegna i dati bibliografici riguardanti le anomalie cervicali in gemelli. La possibilità di un'eredità di anomalie cervicali come le emivertebre non è stata dimostrata. Il caso presentato si pone a sostegno dell'opinione secondo cui la maggior parte di queste anomalie sarebbe causata da fattori periferici non genetici.

RÉSUMÉ

Une paire de jumelles, discordante pour des anomalies spinales cervicales congénitales, est décrite. Les chances de zygosité sont calculées sur la base de la chance initiale de dizygosité, du sexe, des groupes sanguins, des protéines plasmatiques, des enzymes des globules rouges, et des données dermatoglyphiques. La probabilité calculée de monozygosité est de 0.9992. Les données de la littérature concernant des anomalies cervicales chez des jumeaux sont résumées. L'hérédité éventuelle des anomalies spinales, comme les hémivertèbres, n'est pas encore démontrée. Cette paire de jumelles est en faveur de l'opinion que la majorité de ces anomalies soit causée par des facteurs périphériques, non génétiques.

ZUSAMMENFASSUNG

Beschreibung eines weibl. Zwillingspaares mit diskordanten Halswirbelsäulenanomalien. Von der Vermutung ausgehend, es handele sich um ZZ wurden Blutgruppen, Plasma-Proteine, Erythrozytenenzyme u. Hautleisten untersucht und es ergab sich eine EZ-Wahrscheinlichkeit von 0.9992. Es folgt eine Übersicht über die bereits bekannten HWS-Anomalien bei Zwillingen. Die Vererbung solcher Anomalien, wie z.B. Halbwirbel, ist noch nicht bewiesen. Der vorliegende Fall scheint die Ansicht zu stützen, dass der Grossteil dieser Anomalien durch periphere nicht erbbedingte Faktoren bedingt seien.

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