Roentgenologic Abnormalities in Down's Syndrome

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Down 症候群におけるX線所見

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Down 症候群28例のX線写真について，従来より報告されている各種の異常所見の有無および他の新しい異常所見の有無に重点をおいて検討した．異常の大部分は，すでに報告されていると同頻度で認められたが，まれにしか報告されない所見も若干認めた．今回の研究では，脊椎骨計測値の1つに異常が見られたが，これは，Down 症候群における特徴的所見の1つとして追加すべきものであるかもしれない．染色体分析が行なわれた27例全員に本症に一致する染色体異常を認めた．この研究で，日本人についての放射線学的計測に対する正常値の決定の必要が痛感され，また，Down 症候群のX線所見と臨床所見の研究に染色体検査を加えることが望ましいことが指摘された．

Introduction

The Langdon-Down anomaly, congenital acromicria or Trisomy-21 anomaly, referred to in this report as Down's syndrome[1] is more common in Japan than generally realized. Its incidence is at least 0.1% for all live births[2]. Many roentgenological manifestations of Down's syndrome have been studied extensively, but most of these reports involve single or relatively few body sites. The subjects of the present study were observed for all previously reported roentgenological abnormalities in Down's syndrome. Twenty-seven of them had chromosome studies. Three reside with parents in Hiroshima; all others, in

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Nagasaki either with parents or in homes for the handicapped.

Present study

Cases in this study were arbitrarily grouped by age at examination as shown in Table 1. Seventeen of the 28 cases were males; all but 1 were less than 10 years of age, and the majority between 1 and 6.

Roentgenographic projections desirable to demonstrate possible abnormalities are shown in Table 2. These should be borne in mind in observing cases of possible Down's syndrome. Nearly all of the subjects in the present series received these examinations.

Target-film-distances in all cases were 100 cm. No corrections were made for magnification. All roentgenograms were interpreted with emphasis on detection of all abnormalities previously reported in the literature, any possible additional ones, with measurement of structures wherever possible.

Table 1. Distribution of Subjects by Age at Roentgenography Examination and Sex

Age Group	Male	Female	Total
<1 year	3	1	4
1–3	5	4	9
4–6	8	2	10
7–10	1	3	4
Total	17	10(1)	27(1)

( ) = One 20 year old female

Table 2. ROENTGENOLOGICAL EXAMINATIONS

BODY SITES	PROJECTIONS
SKULL	PA, LATERAL
CERVICAL SPINE	AP, LATERAL FLEXION
THORACOLUMBAR SPINE	AP, LATERAL
CHEST	PA, LATERAL, LEFT ANTERIOR OBLIQUE
PELVIS	AP, HIPS IN EXTENSION
HANDS AND WRISTS	PA
FEET	AP

Results

Numbers of observed abnormalities by body site by sex are shown in Table 3. There was some variation in numbers of body sites observed; those inadequately visualized and excluded are shown in parentheses.

Skull Persistence of the metopic suture occurs in 10% of normals according to Kohler and Zimmer[3]. Caffey[4] states it may persist in 8% of normal people after the age of 6 years. Seward et al[5] found persistent metopic sutures in 42% of females and 67% of males with Down's syndrome after the age of 10 years. Spitzer et al[6] found it in one-third of their patients with Down's syndrome. Closure of the metopic suture begins in the second year of life; if closure was not complete by the third year, it was regarded persistent. It was found in 25% of the present series.

Thin calvaria and lack of diploic structures are relatively common in Down's syndrome[4]. Spitzer et al[6] found this in 27 of his 29 cases. Nineteen of 28 cases in the present study had this abnormality.

The skull is ordinarily small and brachycephalic in Down's syndrome. In microcephaly, the head

Table 3. Number of Abnormalities by Body Site Observed, by Sex

	BODY SITE	POSITIVE/OBSERVED MALE	FEMALE
1	Skull metopic suture	3/17	4/11
2	Skull calvaria thin, no diploe	11/17	8/11
3	Skull microcrania	3/17	3/11
4	Skull brachycephaly	15/17	11/11
5	Skull high cribriform	10/17	6/11
6	Skull hypoplastic maxilla	13/17	7/11
7	Skull hypoplastic sinuses	13/17	10/11
8	Skull nasal bone↓ or missing	11/17	7/11
9	Skull teeth deformed, missing, small	8/17	6/11
10	Skull interorbital distance↓	12/17	6/10(1)
11	Spine atlas dislocation, subluxation	0/15(2)	2/11
12	Spine narrow intervertebral spaces	1/16(1)	0/10(1)
13	Spine vertebral body vertical↑, horizontal↓	3/16(1)	5/10(1)
14	Spine vertebral body Schmorl's nodes	0/16(1)	0/10(1)
15	Spine↓ interpedicular distance	4/16(1)	6/9(2)
16	Spine concave ventral edges	10/16(1)	6/10(1)
17	Heart anomaly	1/16(1)	0/10(1)
18	Lung anomaly (Parasternal hernia)	1/17	0/10(1)
19	Wrist bone age accelerated	1/17	0/11
20	Wrist bone age retarded	11/17	5/11
21	Hand fifth digit; terminal phalanx deviated	15/17	8/11
22	Hand fifth digit; middle phalanx hypoplastic	17/17	10/11
23	Hand pseudo-epiphysis	9/17	4/11
24	Pelvis iliac crest, flaring, large	15/17	10/10(1)
25	Pelvis iliac index*	17/17	10/10(1)
26	Pelvis iliac angle*	12/17	6/10(1)
27	Pelvis acetabular angle*	17/17	10/10(1)
28	Pelvis acetabulum flattened	16/17	7/10(1)
29	Pelvis ischium tapering, hypoplastic	5/16(1)	2/10(1)
30	Pelvis coxa valga	5/12(5)	4/9(2)
31	Feet calcaneus two centers	0/10(7)	0/7(4)
32	Feet pseudo-epiphysis	0/10(7)	1/7(4)
33	Feet web	2/13(4)	3/7(4)
34	Eleven ribs	0/17	1/11
35	Maternal age at delivery>30	9/17	7/11
36	Trisomy 21 or translocation	17/17	10/10(1)

**Abnormal and probably abnormal*

( ) = Unknown, no history, no examination or site not visualized.

is small in all diameters, the forehead flat and sloping, and there is prominence of the occipital bone. Some believe this to be due to congenital underdevelopment of the brain in Down's syndrome[7]. Microcephaly was found in 6 of the 28 cases in this study.

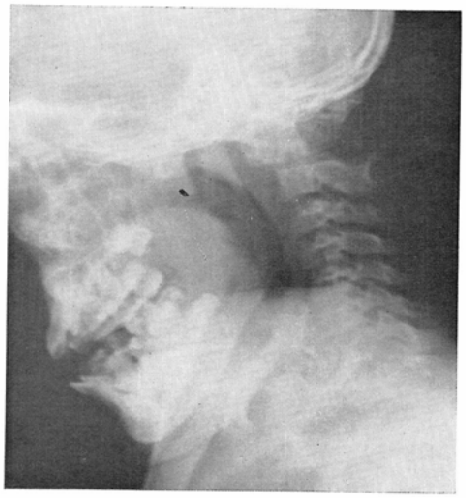
Spitzer et al found brachycephaly in 50% of his cases of Down's syndrome. Twenty-six of the 28 cases in our study were brachycephalic using the measurements of Hass[8]. In Down's syndrome the cribriform plate is often high in the cranial cavity[4]; this was found in 16 of the 28 cases in this study.

Hypoplastic maxillae, sinuses and nasal bones, and other abnormalities were prominent in this, as in other reported series. Less frequently reported in the medical literature, but prominent in our study,

were decreased interorbital distances—in 18 of 27 cases. Measurements were made according to Gerald and Silverman[9].

Spine Two cases of atlanto-axial dislocation were found in this series, similar to those reported by Martel and Tishler[10] and Spitzer et al[6].

Fig. 1 Atlanto-axial dislocation (MF # 745778)



Increased vertical, decreased anteroposterior dimensions of vertebrae, and narrowed intervertebral spaces have been described in Down's syndrome. In the present study, 8 of 26 cases exhibited increased vertical and decreased anteroposterior dimensions. Only 1 of 26 showed narrowed intervertebral spaces.

In this series, there were 10 cases of narrowed interpedicular distances at the lower cervical and upper thoracic levels according to measurements of Simril and Thurston[11]. No other levels of the spine were so involved, and we have been unable to find other reports of this finding in Down's syndrome, of which this could eventually prove to be another stigma.

Sixteen cases had concave anterior vertebral body margins, as previously reported by Rabinowitz and Moseley[12]. In 8 of 26 observed cases, lateral lumbar indices[12] were less than 1.0, but all vertebrae were not equally affected in individual subjects.

Hands and Wrists There has been considerable divergence of opinion as to whether osseous development is delayed, normal, or advanced in Down's syndrome. Using an atlas of normal development[4], 16 of our 28 cases were found retarded, 11 were normal, and 1 case was accelerated in bone maturation. Hefke[13] reported normal bone maturation in 79%, slightly advanced in 14%, and slightly delayed in 7% of his cases.

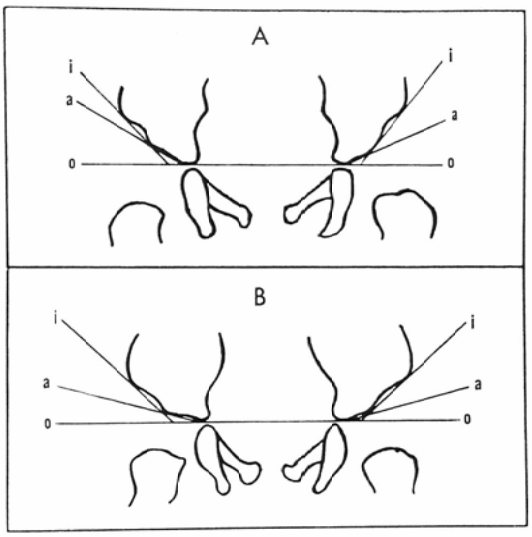
The well-known curvature of the fifth digits of the hands first described by Smith[14] results from hypoplasia of the middle and distal phalanges and deviation of the latter. It is now believed that this finding is specific for Down's syndrome. In 27 of our 28 cases the middle phalanx of the fifth digit was hypoplastic, and in 23 of these there was lateral deviation of the terminal phalanx—bilateral in all cases.

In a large percentage of cases, the first metacarpal, which normally has a proximal epiphysis, also has a distal one. Similarly, the index metacarpal may have a proximal epiphysis in addition to its normal

distal one. Heike[13] found pseudoepiphyses of the first metacarpal in 10% of his series. Thirteen of our 28 cases had pseudoepiphyses of the second metacarpal, but none was found in the first metacarpals.

Pelvis In Down's syndrome, the acetabular angles tend to be flat, and the iliac bones appear wide and flared. The ischial rami are slender and tapered, and there is often bilateral coxa valgae. The roentgenologic abnormalities of the pelvis can be expressed quantitatively by measuring the iliac and acetabular angles, according to the method of Caffey and Ross[15].

Fig. 2 Newborn Pelvic Measurements*



A—Normal B—Down's Syndrome
Acetabular Angle: ao
Iliac Angle: io
Iliac Index: Sum of the two acetabular angles and two iliac angles divided by 2.
* After Caffey[4]

They found that the iliac index, which is the sum of these two angles averaged for the two sides, is a more sensitive indicator of Down's syndrome than either angle considered separately. Their newborn normal iliac index ranged from 65–97°, with a mean of 81° for both sexes. In Down's syndrome their iliac index ranged from 49–80° with a mean of 60°. They concluded these findings are most pronounced during the early months of life when the clinical diagnosis of Down's syndrome is least certain. These roentgenologic diagnoses are reasonably certain in 80% cases; suggestive in 20%; and uncertain or normal in less than 5%. Kaufmann[16] reported these abnormal configurations of the pelvis persist throughout life.

Astley[17] suggested grading pelvic roentgenological findings in Down's syndrome patients from birth to 8 years, as follows:

1. Under 60°—Down's syndrome highly probable.
2. Between 68° and 60°, Down's syndrome probable (10% of normals included).
3. 68° to 78° Down's syndrome improbable (6% of Down's syndrome included).
4. Over 78°, probably normal.

Pelvic roentgenological abnormalities in our series classified according to these authors are shown in Table 4.

As frequently reported by others, the majority of subjects in this series had flared iliac crests, and decreased iliac and acetabular angles. The iliac index was abnormally low in all cases. There were variations in the degree of contribution by measurements on which the iliac index is based, but the acetabular angle was the most significant contributor to the low iliac index. The ischium was tapered in 7 of 26 cases, and coxa valga was observed in 9 of 21.

Table 4. Ranges of Pelvic Measurements*; Number of Cases by Sex

	Male	Female	Total		
Iliac index≦60°	12	5(1)	17(1)	17(1)	Abnormal
60<Iliac index≦68°	3	5	8	10	Probably abnormal
68<Iliac index≦78°	2	0	2		
Iliac index>78°	0	0	0	0	Normal
7≦Acetabular angle≦12°	8	5(1)	13(1)	13(1)	Abnormal
12<Acetabular angle≦25°	9	5	14	14	Probably abnormal
25<Acetabular angle≦37°	0	0	0	0	Normal
30<Iliac angle≦44°	12	6	18(1)	18	Abnormal
44<Iliac angle≦56°	4	3	7	7	Probably abnormal
56≦Iliac angle≦66°	1	1	2	2	Normal

( ) = Unknown; site not visualized, or not examined.
*According to Astley[17]
Iliac index based on Caffey and Ross[15]

Other X-Ray Observations All patients with Down's syndrome should be observed carefully for other anomalies; 5 of the 28 cases in the present series had such. Chest roentgenograms of 1 case showed a parasternal hernia. Findings suggestive of a cardiac anomaly, probably interventricular septal defect, were seen in another. One case had eleven ribs bilaterally; another, a cleft palate. One case had had surgical correction of congenital anal atresia. Five of 20 observed had "web" foot deformities or broad feet.

Chromosome Abnormalities and Other Observations Patients in this study are shown in Table 5 by master file number, chromosome abnormality and family histories. G-Trisomy is the most frequent chromosome abnormality in Down's syndrome, but D/G and G/G translocations have also been found. Of the 27 subjects with chromosome studies, 25 had G-Trisomy; one each, D/G and G/G translocations. Maternal age at birth of the child ranged from 22 to 46 years, with an average age of 33 years.

The mother of 1 subject experienced the Hiroshima A-bomb at 3-months gestation. She was located 1,400 meters from the hypocenter and is estimated to have received 27 rads. Correlation of this condition and A-bomb exposure could not be established. This case was in a chromosome study previously reported[18].

Table 5. Patients by Chromosome Abnormality and Family History

MF #	Sex	Birth date	Age at patient's birth		Live birth rank / Number of sibs
			Paternal	Maternal	
G-Trisomy					
733659	M	7 Nov 61	26	28	1/2 (Twin)
737389	M	25 Jan 63	26	22	1/2
737925	F	5 Aug 63	48	42	4/4
738702	F	9 Apr 63	34	31	2/2
738703	F	1 Mar 64	30	27	2/2
739258	M	27 Jul 64	29	28	1/1
739282	M	15 Jan 62	36	28	2/2
739863	M	24 May 60	50	39	1/1
741749	F	30 Nov 59	32	32	1/3
742274	M	7 Aug 61	33	32	2/2
743947	F	8 May 64	36	30	2/3
744325	F	30 Nov 60	35	25	2/2
744326	M	25 Feb 62	44	39	3/3
744463	M	13 Sep 66	30	29	3/3
744464	M	24 Apr 61	38	32	3/3
744712	M	13 Aug 66	42	39	3/3
745149	M	30 Jan 64	30	26	1/1
745756	F	11 Sep 60	46	36	6/7
745759	M	16 Oct 61	33	32	1/3
745779	M	2 Oct 58	44	38	7/7
745778	M	7 Jun 61	42	38	7/9
745911	F	14 Sep 62	49	40	5/5
745916	F	28 Jan 58	26	25	1/3
404032	F	23 Jan 46	64	46	3/3
403929	M	18 Aug 45	50	41	5/5
D/G Translocation					
738122	M	19 Sep 60	34	28	2/2
G/G Translocation					
744840	M	1 Mar 66	25	24	1/1
No Examination					
314148	F	29 Jan 52	38	35	4/4
Average parental age at child birth			37.5	32.6	

Discussion

Roentgenological abnormalities observed in this study were for the most part qualitatively and quantitatively similar to those reported elsewhere. Most frequent abnormalities were found in the pelvis, followed by deformities of the fifth digits of the hands, and brachycephaly, in that order. However, some less frequently reported abnormalities were also seen; such as atlanto-axial dislocation, disproportion of vertebral body measurements, and concave ventral margins of vertebrae. Interorbital distances were less than normal in 65% of our cases, and bone maturation delayed in 55%. One finding not previously reported in Down's syndrome, but seen in 40% of the present series, was decreased interpedicular distances at the 7th cervical level. This eventually could prove to be a diagnostic feature of Down's syndrome if found consistently in other studies in the future.

Roentgenological measurements in the present study were assessed by norms compiled for other

populations, since none exist for the Japanese. Use of these norms for skull and spine evaluations may be questioned, since some measurements could be a reflection of the generally smaller stature of the Japanese compared to members of other populations. This demonstrates the need for norms for the Japanese.

Chromosome abnormalities consisted of 25 cases of G-Trisomy and 2 cases of translocations. There was no correlation of types of roentgenological and chromosome abnormalities. As in other Japanese series studied cytogenetically, over 90% of abnormalities consisted of G-Trisomy.

Chromosome studies that demonstrate the presence of excess 21 material will usually confirm a diagnosis of Down's syndrome. Occasionally, especially in mosaicism, chromosome abnormalities may not be detectable in peripheral blood cultures.

Acute infectious hepatitis has a teratogenic effect and may result in Down's syndrome[19]. No such correlation was established among mothers of the patients in this series.

Summary

Roentgenograms of 28 patients with Down's syndrome were reviewed with emphasis on all previously reported abnormalities and any possible additional ones. Most of the abnormalities occurred with the same frequency as previously reported, but some less frequently reported findings were also seen. One abnormal vertebral measurement found in this series may be an additional stigma of Down's syndrome. All of the 27 cases studied cytogenetically had chromosomal abnormalities consistent with this disease. This study emphasizes the need for roentgenologic norms for the Japanese, and the desirability of combining chromosome studies with roentgenological abnormalities and clinical observations in diagnosing Down's syndrome.

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