Jpn J Human Genet 38, 209–217, 1993

Case Report

TWO JAPANESE CASES WITH MICROCEPHALIC PRIMORDIAL DWARFISM: CLASSICAL SECKEL SYNDROME AND OSTEODYSPLASTIC PRIMORDIAL DWARFISM TYPE II

Yoshitsugu SUGIO,* Masato TSUKAHARA, and Tadashi KAJII

Department of Pediatrics, Yamaguchi University School of Medicine, Ube 755, Japan

Summary A male infant with "classical" Seckel syndrome and a girl with osteodysplastic primordial dwarfism type II are described. The boy with classical Seckel syndrome had severe brain dysplasia, a finding hitherto unreported in patients with this syndrome. The patient with osteodysplastic dwarfism type II had skeletal abnormalities including lumbar scoliosis, a small and high pelvis, metaphyseal flaring of the distal radii and ulnae, V-shaped metaphyseal flaring of the distal femorae, and short metacarpals and phalanges. The mother of this girl was short, microcephalic, and had disproportionately short forearms and legs. In view of this, dominant inheritance of the disease was suggested.

Key Words Seckel syndrome, osteodysplastic primordial dwarfism type II

INTRODUCTION

The term "bird-headed dwarfism" was coined by Seckel (1960) in reviewing 15 individuals with severe microcephaly and dwarfism: 2 personally observed and 13 from the literatures. Since then, many case reports have appeared under various terms such as bird-headed dwarfism, Seckel dwarfism or Seckel syndrome.

Majewski and Goecke (1982), in reviewing 60 such patients, found only 17 to meet their criteria for "classical" Seckel syndrome. The criteria included 1) marked intrauterine growth retardation (birth weight below 2,055 g), 2) postnatal growth retardation (below −5 S.D.), 3) severe microcephaly (below −4 S.D.), 4) severe mental retardation, and 5) bird-headed facial appearance. These authors delineated three subtypes of bird-headed primordial dwarfism distinct from "classical" Seckel syndrome, referred to respectively as osteodysplastic primordial dwarf-

Received November 4, 1992; Revised Accepted April 6, 1993.

*Present address and reprint request to: Yoshitsugu Sugio, M.D., Pediatric Clinic, Ogori Daiichi Hospital, 862–3, Shimogo, Orogicho, Yoshikigun, Yamaguchi 754, Japan.

ism types I, II, and III (Majewski and Spranger, 1976; Majewski *et al.*, 1982a, b). The differentiating features of type I osteodysplastic promordial dwarfism were a broad, low "dysplastic" pelvis with poor acetabular development, and disproportionately short, broad, and bowed humeri and femora. The main features of type II osteodysplastic dwarfism include short limbs, coxa vara, epiphysiolysis, metaphyseal flaring, and V-shaped distal femoral metaphyses. Those of type III osteodysplastic dwarfism were proportionate dwarfism, platyspondyly, long dysplastic clavicles, hypoplasia of iliac wings and acetabula, and broad femora. Types I and III were later lumped together (Meinecke and Passarge, 1991), and other types of bird-headed dwarfism have since been described (Fitch *et al.*, 1970; Bangstad *et al.*, 1989).

We report here an infant with "classical" Seckel syndrome and a child with type II osteodysplastic primordial dwarfism.

CASE REPORTS

The clinical data of the two patients are summarized in Tables 1 and 2.

Patient 1 (No. 831189) was born in 1983 at term to a 34-year-old, gravida III, para II mother and a 36-year-old father, both healthy and unrelated. There was neither a history of viral infection nor of X-ray exposure during the pregnancy. The mother was involved in a traffic accident at 5 weeks of pregnancy, and took sulfamethoxazole and triamide for a week. A 7-year-old brother and 4-year-old sister were both phenotypically normal. The patient was fed nasally in an incubator with 35% oxygen during the neonatal period.

When first seen by us at age 40 days, the patient weighed 1,374 g and measured 37.4 cm. He was severely microcephalic and very short but proportioned (Fig. 1). He had a bird-headed facial appearance with a receding forehead and chin, a beaklike nose with a prominent root, large eyes, and large and simple ears (Fig. 2). His anterior fontanel was closed. Also noted were sparse hair, a narrow

Table 1. Clinical data of two patients.

	Patient 1	Patient 2
Age (yr) at examination	11/12	3
Sex	M	F
Birth weight (g) (S.D.)	920 (−5.6)	1,520 (−1.6)
Birth height (cm) (S.D.)	29 (−9.6)	40 (−1.0)
Birth OFC (cm) (S.D.)	19.5 (−16.0)	28 (−1.3)
Weight (kg) (S.D.)	2.5 (−6.8)	8.0 (−3.9)
Height (cm) (S.D.)	51.9 (−8.8)	84 (−2.6)
OFC[a] (cm) (S.D.)	28.4 (−11.9)	43.3 (−5.2)
Arm span length (cm)		77.8

[a] OFC, occipito-frontal circumference.

Table 2. Clinical features of two patients.

	Patient 1	Patient 2
	Classical Seckel syndrome	Osteodysplastic primordial dwarfism type II
Growth		
Prenatal onset growth retardation	+	−
Postnatal growth retardation	+	+
Delayed osseous maturation	+	+
Mental retardation	+	+
Craniofacial		
Craniosynostosis	+	−
Relatively large ears	+	−
Malformed ears	+	+
Downslanting palpebral fissures	−	−
Prominent curved nose	+	−
Micrognathia	+	+
Highly arched palate	+	+
Cleft palate	−	−
Enamel hypoplasia	?	−
Limbs		
Disproportionate short forearms	−	+
Clinodactyly	+	+
Dislocation of radial head	−	−
Genitalia		
Cryptorchidism	−	
Clitolomegaly		−
Skin		
Hirsutism	−	−
Roentgenographic findings		
Brachymesophalangy	−	+
Brachymetacarpy I	−	+
Flared distal femoral metaphyses	−	+
Triangular shape of the distal femoral epiphyses	−	+
High and narrow pelvis	−	+
Proximal femoral epiphysiolysis	−	−
Coxa vara	−	−
Others	Hydronephrosis	Soft tissue syndactyly II–III, III–IV toes Agenesis right kidney

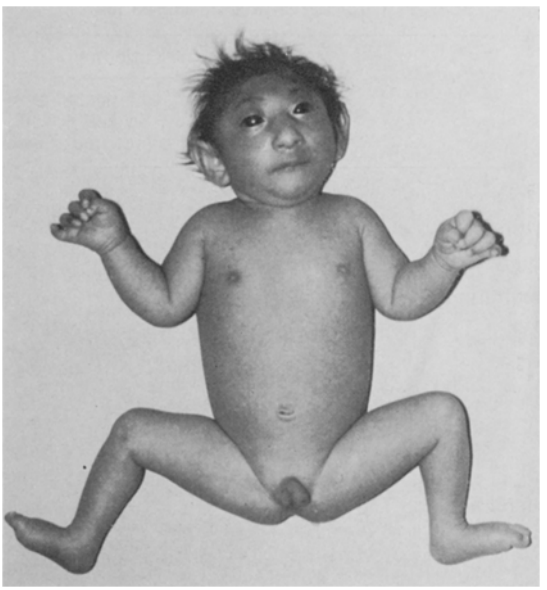

Fig. 1. Patient 1 at age 2 months.

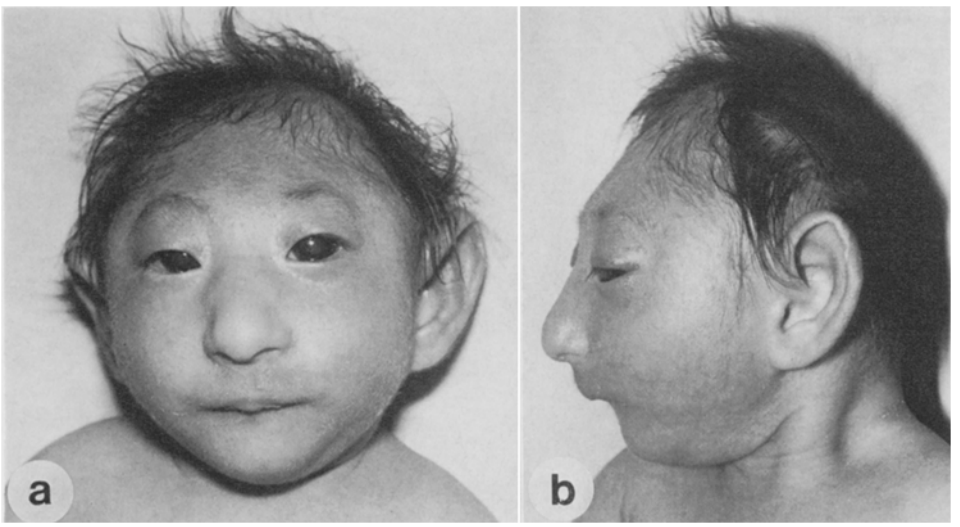

Fig. 2. Frontal view (a) and profile (b) of patient 1 at age 2 months.

palate, a short sternum, white pupils, tapering fingers, clinodactyly of the fifth fingers with single flexion creases, and limitation of extention of the shoulder, elbow, hip, and knee joints. At age 4 months, a complete skeletal survey revealed absence of ossification of the distal femoral heads. The pelvis, vertebrae, and metaphyses

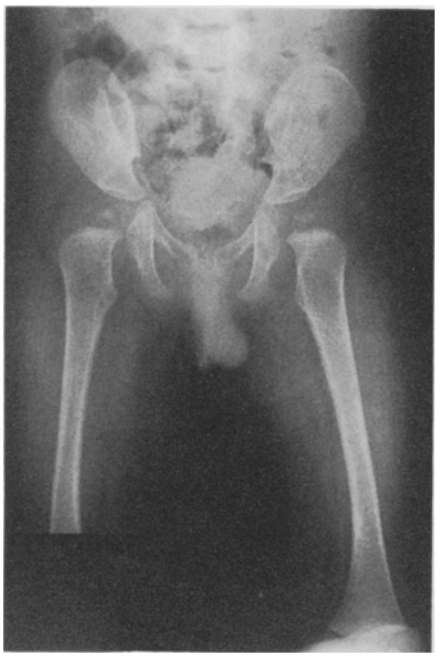

Fig. 3. Roentgenograms of the pelvis and femorae in patient 1 at age 11 months.

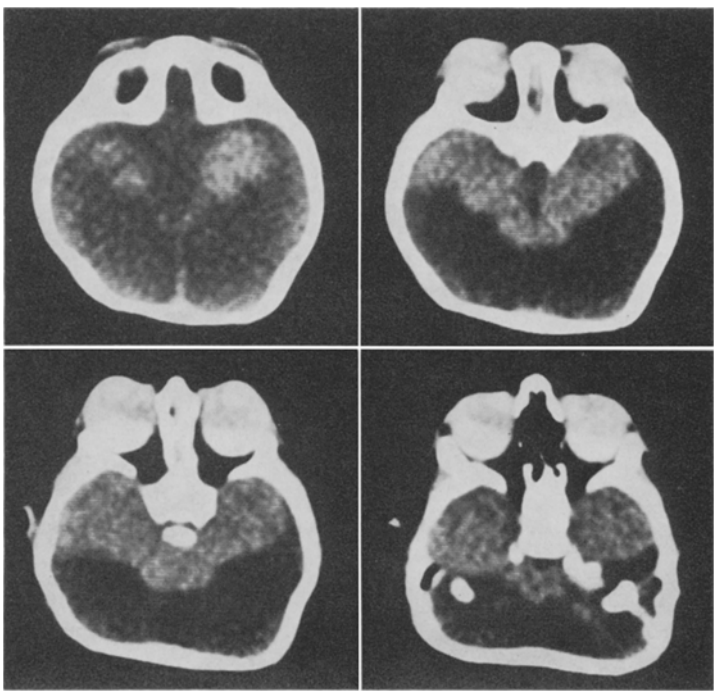

Fig. 4. Brain CT scan of patient 1 at age 2 months, taken in 1982.

of the long bones were grossly normal (Fig. 3). Brain CT scan at age 2 months revealed hypoplastic cerebrum and cerebellum resulting in a largely empty intracranial space (Fig. 4). Intraveous pyelography showed left hydronephrosis. Funduscopic examination revealed bilateral retrolental fibroplasia. G-banded chromosomes were 46,XY.

At age 11 months, he neither smiled, nor rolled over. At age 22 months, he died at home after a 1-week illness. Autopsy was not granted.

Patient 2 (No. 1016064) was born by cesarean section after 34 weeks of gestation to a 31-year-old gravida III, para II mother and a 33-year-old father, both healthy and unrelated. Bilateral soft tissue syndactyly between the second and third toes and between the third and fourth toes were surgically repaired at age 16 months.

When first seen at 3 years, she was short (-2.6 S.D.) and microcephalic (-5.2 S.D.) (Fig. 5). Her forearms and legs were disproportionately short. She had a broad nasal root continuous from the forehead, hypoplastic alae nasi, a right low-set ear, simple ears, a small mouth, and micrognathia (Fig. 6). She had clinodactyly of the fifth fingers. A complete skeletal survey revealed lumbar scoliosis, a small and high pelvis, mild metaphyseal flaring of the distal radii and ulnae, V-shaped metaphyseal flaring of the distal femorae, and short metacarpals and phalanges (Fig. 7). Her carpal bone age was 18 months. Brain CT scan was normal. Intravenous pyelography revealed agenesis of the right kidney. Her developmental

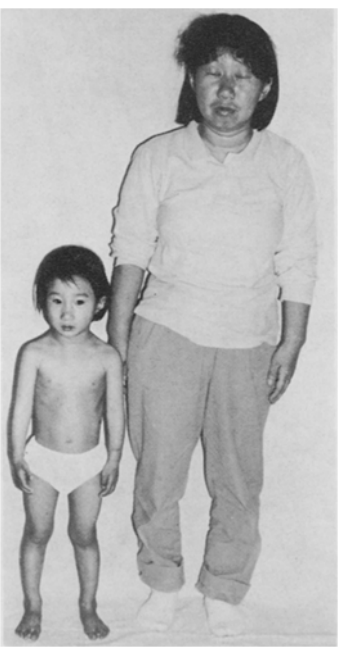

Fig. 5. Patient 2 at 3 years and her mother.

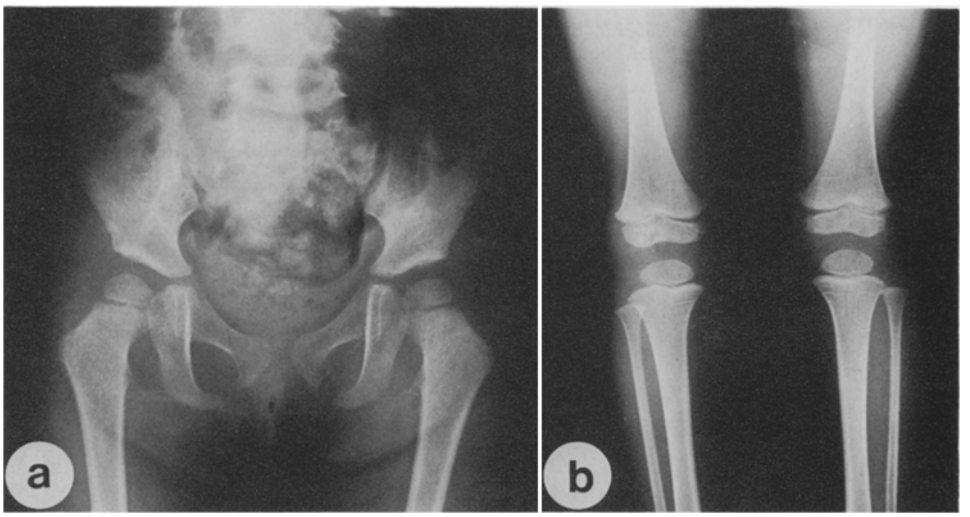

Fig. 6. Frontal view (a) and profile (b) of patient 2.

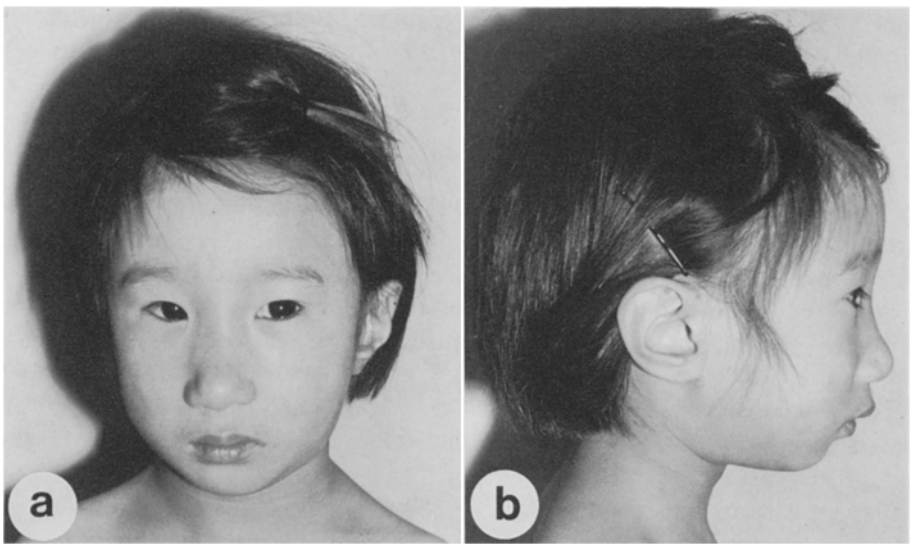

Fig. 7. Roentgenograms of patient 2 showing small and high pelvis (a) and V-shaped metaphyseal flaring of the distal femorae (b).

quotient was 70. G-banded chromosomes were 46,XX.

Family members. The father was phenotypically normal with a height of 169 cm. The mother measured 134.5 cm (−4.4 S.D.), weighed 41 kg (−1.7 S.D.), and her head circumference was 51.5 cm (−1.9 S.D.). She was reported to be "born small." Her arm span length was 125.6 cm and she had small hands and

feet (Fig. 1). Her skeletal survey was not granted. Both parents were high-school graduates and were of normal intelligence. Two elder brothers, 11 and 13 years of age, were phenotypically normal.

DISCUSSION

Patient 1 we described showed the clinical manifestations of classical Seckel syndrome with severe pre- and post-natal growth retardation, severe microcephaly, severe mental retardation and a "bird-headed" facial appearance. His brain showed marked dysplasia, a finding hitherto undescribed in patients with classical Seckel syndrome. To our knowledge, 19 patients with classical Seckel syndrome have been reported (17 cases reviewed by Majewski and Goecke, 1982; 2 by Butler *et al.*, 1987). At least 9 Japanese patients have been published as Seckel syndrome (Fukuda *et al.*, 1991). None of them fulfils the criteria proposed by Majewski and Goecke (1982).

Patient 2 meets the diagnostic criteria of type II osteodysplastic dwarfism with postnatal dwarfism, microcephaly, and disproportionately short forearms and legs, and also with various skeletal abnormalities including lumbar scoliosis, a small and high pelvis, metaphyseal flaring of the distal radii and ulnae, V-shaped metaphyseal flaring of the distal femorae, short metacarpals and phalanges, and delayed osseous maturation. To our knowledge, 8 patients with type II osteodysplastic dwarfism have been reported, including a pair of affected sibs from consanguineous parents (Majewski *et al.*, 1982a; Verloes *et al.*, 1987; Willems *et al.*, 1987). This disorder is thus considered to be autosomal recessive. However, the mother of patient 2 had several manifestations of the disorder, including short stature, a short arm span, microcephaly, and small hands. Assuming that she was mildly affected, the possibility that this disorder is inherited in a dominant fashion in this family cannot be ruled out.

Acknowledgments We thank Dr. S. Kaya (Pediatric Clinic, Tokuyama Chuo Hospital) and Dr. Suenaga (Pediatric Clinic, Shimonoseki City Chuo Hospital) for referring patients 1 and 2, respectively.

REFERENCES

Bangstad H-J, Beck-Nielsen H, Hother-Nielsen O, Nystad R, Trygstad O, Pedersen O, Aagenaes O (1989): Primordial bird headed nanism associated with progressive ataxia early onset insulin resistant diabetes, goiter, and primary gonadal insufficiency. Acta Paediatr Scand **78**: 488–493

Butler MG, Hall BD, Maclean RN, Lozzio CB (1987): Do some patients with Seckel syndrome have hematological problems and/or chromosome breakage? Am J Med Genet **27**: 645–649

Fitch N, Pinsky L, Lachance RC (1970): A form of bird-headed dwarfism with features of premature senility. Am J Dis Child **120**: 260–264

Fukuda S, Morishita Y, Hashiguchi M, Taira A (1991): Seckel syndrome associated with atrial septal defect; a case report and review of the literature in Japan. Kyobugeka **44**: 411–413 (in Japanese)

Meinecke P, Passarge E (1991): Microcephalic osteodysplastic primordial dwarfism type I/III in sibs. J Med Genet **28**: 795–800

Majewski F, Spranger J (1976): Über einen neuen Typ des primordialen Minderwuchses: Der brachymele primordiale Minderwuchs. Mschr Kinderheilk **124**: 499–503

Majewski F, Goecke T (1982): Studies of microcephalic primordial dwarfism I: approach to a delineation of the Seckel syndrome. Am J Med Genet **12**: 7–21

Majewski F, Ranke M, Schinzel A (1982a): Studies of microcephalic primordial dwarfism II: the osteodysplastic type II of primordial dwarfism. Am J Med Genet **12**: 23–35

Majewski F, Stoeckenius M, Kemperdick H (1982b): Studies of microcephalic primordial dwarfism III: an intrauterine dwarf with platyspondyly and anomalies of pelvis and clavicles—osteodysplastic primordial dwarfism type III. Am J Med Genet **12**: 37–42

Seckel HPG (1960): Bird-headed dwarfs. Charles C. Thomas, Springfield, pp 1–241

Verloes A, Lambrechts L, Senterre J, Lambotte C (1987): Microcephalic osteodysplastic dwarfism (type II-like) in siblings. Clin Genet **32**: 88–94

Willems PJ, Rouwé C, Smit GPA (1987): A new case of the osteodysplastic primordial dwarfism type II. Am J Med Genet **26**: 819–824