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A JAPANESE MALE INFANT WITH THE WEAVER SYNDROME

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Summary A 15-month-old male infant who had pre- and postnatal overgrowth, accelerated bone maturation and characteristic facial appearance was described. Although a Japanese female with Weaver syndrome previously reported had slightly different clinical manifestations from others, our patient had typical clinical features of Weaver syndrome. We suggest that a genetic mutation of the syndrome may be the same in Japanese as other ethnic groups and that Weaver syndrome may be an autosomal dominant disorder with variable expressions.

Key Words Weaver syndrome, Japanese, overgrowth, accelerated bone maturation

INTRODUCTION

Since Weaver *et al.* (1974) first described two patients with overgrowth and unusual facies, 28 patients with the Weaver syndrome have been reported (Weaver, 1990; Moreno and Kirkland, 1974; Bosch-Banyeras *et al.*, 1978; Shimura *et al.*, 1979; Gemme *et al.*, 1980; Majewski *et al.*, 1981; Weisswichert *et al.*, 1981; Meinecke *et al.*, 1983; Jalaguier, 1983; Roussounis and Crawford, 1983; Amir *et al.*, 1984; Farrell and Hughes, 1985; Ardinger *et al.*, 1986; Greenberg *et al.*, 1989). However, clinical manifestations of some patients including a Japanese were similar to those of other overgrowth syndromes such as Marshall-Smith and Beckwith-Wiedemann syndromes (Shimura *et al.*, 1979; Menguy *et al.*, 1986; Pattenati *et al.*, 1986). These patients made it difficult to make a diagnose of Weaver syndrome and question whether the syndrome is distinct have been discussed (Fitch, 1980, 1985; Cohen Jr., 1988). Further reports have been needed to delineate the phenotypic spectrum of anomalies.

We present here a Japanese male infant with typical clinical manifestations

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of Weaver syndrome. Although ethiology of Weaver syndrome is unclear, Japanese patients with Weaver syndrome have the same mutation in other ethnic groups. A gene expression in another Japanese patient (Shimura *et al.*, 1979) might be modified by other factors.

CASE REPORT

The 15-month-old infant is the first and only child of healthy and unrelated parents. The 29-year-old mother and 30-year-old father were 152 cm and 175 cm tall, respectively. During the third trimester of the pregnancy, there was excessive uterine enlargement and the patient was delivered by cesarean section at 40 weeks of gestation. Birth weight, length, and head circumference were 4,250 g, 51.5 cm, and 35 cm. His growth curve followed over 97th percentile in weight, length, and head circumference. The motor development was mildly delayed.

Physical examination at the age of 11 months revealed that his weight, length and head circumference were 13 kg (<97th centile), 84.0 cm (<97th centile), and 48.5 cm (<97th centile), respectively (Fig. 1). Dysmorphic facies were: sparse hair, broad forehead, flat occiput, broad eyebrows, broad and depressed nasal root, mild hypertelorism, depressed nose, and large ears (Fig. 2a, b). The developmental quotient was 64 by Tsumori and Isobe Scale of Developmental Maturity

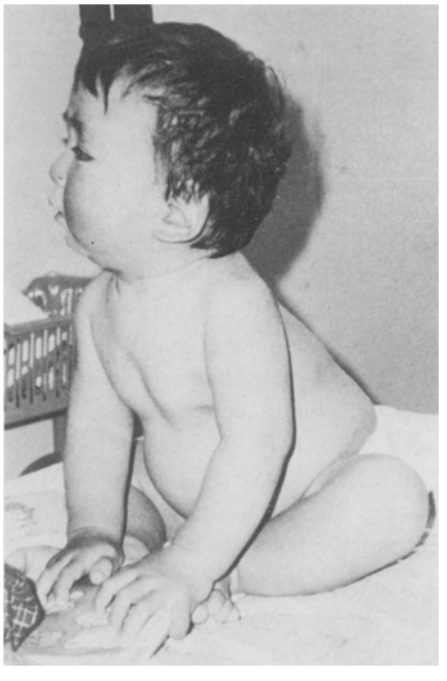

Fig. 1. Patient at 11 months of age.

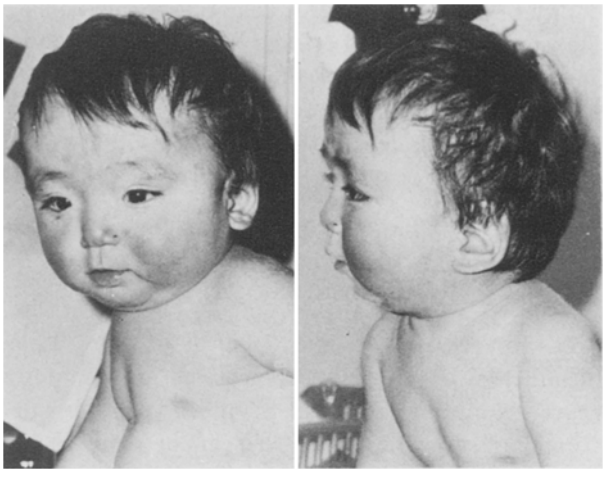

Fig. 2. Facial appearance showing broad forehead, broad nasal bridge, long accentuated philtrum, small mouth, micrognathia and large ears.

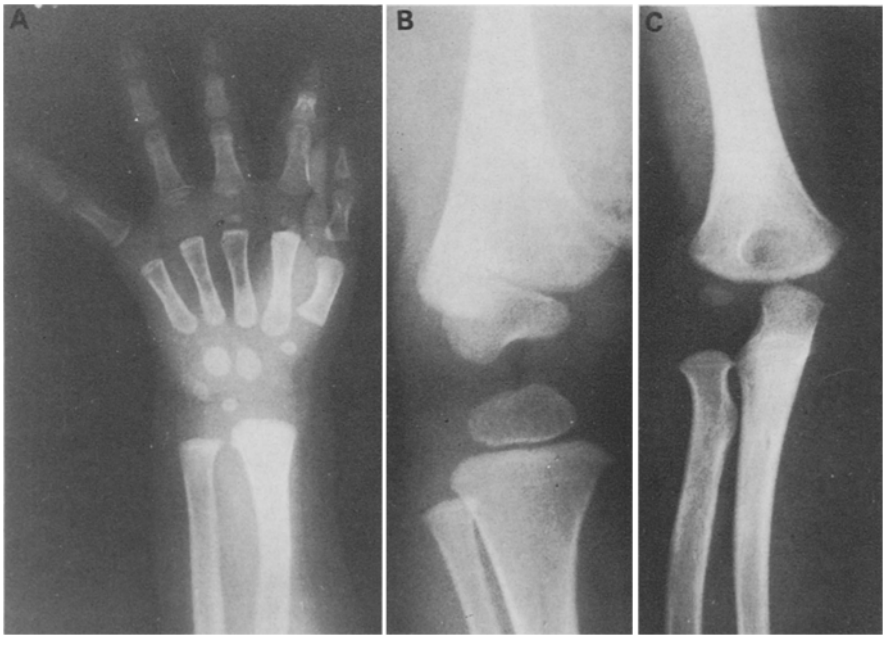

Fig. 3. Radiographs of the patient. Hand of the patient at 11 months of age, showing dysmorphic accelerated osseous maturation (A), and femurs (B) and humerus (C) showing widened metaphyses.

(1981). Camptodactyly of the second fingers and long fourth fingers were noted (Fig. 1). Cardiac murmur was not noted. Liber and spleen were not palpable.

Laboratory data including chromosome analyses using high resolution banding

technique (Ikeuchi and Sasaki, 1979), growth hormone and somatomedine C levels were normal. However, TSH and T3 levels were elevated and total cholesterol levels was 189 mg/dl. Radiographs of the hands revealed that carpal bone age was corresponded to 5 years (Fig. 3A) and splaying of the distal parts of femur (Fig. 3B), tibia (Fig. 3B), and humerus (Fig. 3C) were observed. Dermatoglyphics showed normal palmar creases and 10 whols. Palmar axial triradii were in the t position.

DISCUSSION

Recently, Cohen Jr. (1988) presented clinical features of Weaver syndrome and stated that characteristic facial appearance was most important clinical manifestations of Weaver syndrome. Clinical manifestations of patients with Weaver syndrome were summarized in Table 1. The patient reported here had strikingly

Table 1. Clinical features of patients with Weaver syndrome.

Findings	Frequency	Our patient
Growth		
Prenatal growth excess	19/26	+
Postnatal growth excess	26/26	+
Accelerated osseous maturation	20/20	+
Performance		
Hypertonia	10/18	+
Mild developmental delay	20/20	+
Hoarse low-pitched cry	14/17	+
Craniofacial		
Broad forehead	20/21	+
Flat occiput	5/13	+
Large ears	23/24	+
Ocular hypertelorism	23/24	+
Prominent or long philtrum	19/24	+
Relative micrognathia	22/22	+
Limbs		
Camptodactyly	11/16	+
Prominent fingerpads	12/13	+
Broad thums	4/ 6	−
Clinodactyly, toes	4/ 5	−
Limited elbow or knee extension	10/13	−
Widened distal long bones	16/18	+
Others		
Short neck with excess loose skin	11/12	+
Umblical hernia	12/17	−

similar facial appearance to the two original patients (Weaver *et al.*, 1974). In the literature, two Japanese patients with Weaver like syndrome were reported (Shimura *et al.*, 1979; Tsukahara *et al.*, 1984). However, the patient reported by Shimura *et al.* (1979) was diagnosed originally as having Marshall-Smith syndrome and she never had overgrowth. The patient reported by Tsukahara (1984) was reexamined and was diagnosed as the Golabi-Rosen syndrome (Kajii and Tsukahara, 1984). Therefore, this is the first report of Japanese patient with typical Weaver syndrome.

The etiology of the Weaver syndrome is unclear. Chromosome analyses were performed in two patients and revealed normal (Weisswichert *et al.*, 1981; Ardinger *et al.*, 1986). High resolution banding chromosome analysis in our patient showed normal male karyotype. Positive family histories have been reported in 4 patients: two sib pairs (Jalaguier, 1983; Roussounis and Crawford, 1983) and two pairs of mother and son (Majewski *et al.*, 1981; Ardinger *et al.*, 1986). The mean paternal age at birth of patients was 31.2 years (Ardinger *et al.*, 1986). Males were more affected, sex ratio: 4M/1F. Clinical features were variable. However, female patients with Weaver syndrome had typical facial appearance of the syndrome (Meinecke *et al.*, 1983; Ardinger *et al.*, 1986). These findings suggest that the ethiology of Weaver syndrome may be a genetic mutation with autosomal dominant inheritance.

REFERENCES

Amir, N., Gross-Kieselstein, E., Hirsch, H.J., Lax, E. and Silverberg-Shalev, R. 1984. Weaver-Smith syndrome: A case study with long-term follow-up. *Am. J. Dis. Child.* **138**: 1113–1117.

Ardinger, H.H., Hanson, J.W., Harrod, M.J.E., Cohen, M.M., Jr., Tibbles, J.A.R., Welch, J.P., Young-Wee, T., Sommer, A., Goldberg, R., Shprintzen, R.J., Sidoti, E.J., Leichtman, L.G. and Hoyme, H.E. 1986. Further delineation of Weaver syndrome. *J. Pediatr.* **108**: 228–235.

Bosch-Banyeras, J.M., Salcedo, S., Lucaya, J., Laverde, R., Boronat, M. and Marti-Henneberg, C. 1978. Acceleration du developpement postnatal, hypertonie, enlargissement des phalanges medianes et des metaphyses distales du femur, facies particulier: sagit il d'un syndrome de Weaver? *Arch. Fr. Pediatr.* **35**: 177–183.

Cohen, M.M., Jr. 1988. A comprehensive and clinical assessment of overgrowth and overgrowth syndromes. In *Advances in Human Genetics 18*. Harris, H. and Hirshhorn, K., eds., Plenum Press, New York and London, pp. 181–303.

Farrell, S.A. and Hughes, H.E. 1985. Brief clinical report: Weaver syndrome with pes cavus. *Am. J. Med. Genet.* **21**: 737–739.

Fitch, N. 1980. The syndromes of Marshall and Weaver. *J. Med. Genet.* **17**: 174–178.

Fitch, N. 1985. Updata on the Marshall-Smith-Weaver controversy. *Am. J. Med. Genet.* **20**: 559–562.

Gemme, G., Bonioli, E., Ruffa, G. and Lagorio, V. 1980. The Weaver-Smith syndrome. *J. Pediatr.* **97**: 962–964.

Greenberg, F., Wasiewski, W. and McCabe, E.R.B. 1989. Weaver syndrome: The changing phenotype in an adult. *Am. J. Med. Genet.* **33**: 127–129.

Ikeuchi, T. and Sasaki, M. 1979. Accumulation of early mitotic cells in ethidium bromide-treated human lymphocyte cultures. *Proc. Jpn. Acad.* **55**: 15–18.

Jalaguier, J., Montoya, F., Germain, M. and Bonnet, H. 1983. Advance de la maturation osseuse et

syndrome dysmorphique chez duex germains (syndrome de Marshall-Weaver). *J. Genet. Hum.* **31**: 385–395.

Kajii, T. and Tsukahara, M. 1984. The Golabi-Rosen syndrome. *Am. J. Med. Genet.* **19**: 819.

Majewski, F., Ranke, M., Kemperdick, H. and Schmidt, E. 1981. The Weaver syndrome: A rare type of primordial overgrowth. *Eur. J. Pediatr.* **137**: 277–282.

Meinecke, P., Schaefer, E. and Engelbrecht, R. 1983. The Weaver syndrome in a girl. *Eur. J. Pediatr.* **141**: 58–59.

Menguy, C., Rival, J.M., Plisson-Salomon, A.S., Barfier, M.L. and Fournet, J.P. 1986. Le syndrome de Marshall. *Ann. Prdiatr.* **33**: 339–343.

Moreno, H. and Kirkland, R. 1974. Another candidate for the overgrowth syndrome (letter). *J. Pediatr.* **85**: 583.

Pettenati, M.J., Haines, J.L., Higgins, R.R., Wappner, R.S., Palmer, C.G. and Weaver, D.D. 1986. Wiedemann-Beckwith syndrome: Presentation of clinical and cytogenetic data on 22 new cases and review of the literature. *Hum. Genet.* **74**: 143–154.

Roussounis, S.H. and Crawford, M.J. 1983. Siblings with Weaver syndrome. *J. Pediatr.* **102**: 595–597.

Shimura, T., Utsumi, Y., Fujikawa, S., Nakamura, H. and Baba, K. 1979. Marshall-Smith syndrome with large bifrontal diameter, broad distal femora, camptodactyly, and without broad middle phalangs. *J. Pediatr.* **94**: 93–95.

Tsukahara, M., Tanaka, S. and Kajii, T. 1984. A Weaver-like syndrome in a Japanese boy. *Clin. Genet.* **25**: 73–78.

Tsumori, M. and Isobe, K. 1981. *Developmental Screening Test for Infants* (in Japanese). Dai-nippon-Tosho Co., Tokyo.

Weaver, D.D., Graham, C.B., Thomas, I.T. and Smith, D.W. 1974. A new overgrowth syndrome with accelerated skeletal maturation, unusual facies, and camptodactyly. *J. Pediatr.* **84**: 547–552.

Weaver, D.D. 1990. Personal communication.

Weisswichert, P.H., Knapp, G. and Willich, E. 1981. Accelerated bone maturation syndrome of the Weaver type. *Eur. J. Pediatr.* **137**: 329–333.