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A Case of Medulloblastoma Associated with Rubinstein-Taybi Syndrome

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=Abstract=**A case of medulloblastoma associated with Rubinstein-Taybi syndrome is reported, as this is the first reported case of medulloblastoma associated with this syndrome, to our knowlegde. The patient was an 8 1/2-year-old girl who had a typical facial appearance, broadening of the thumbs and great toes, and mental retardation. She had been exhibiting irritability for one month. A brain CT scan showed a homogeneously enhanced round mass in the midline of the posterior fossa with marked hydrocephalus. Gross total removal of the mass was performed, and the pathology showed findings of medulloblastoma.**

Key Words: *Medulloblastoma, Rubinstein-Taybi syndrome (RTS)*

INTRODUCTION

Rubinstein-Taybi syndrome (RTS) is characterized by mental retardation, broadening of the thumbs and great toes, and a typical facial appearance. The cause is not yet known. The first description of a patient with RTS was probably given by Michail, Matsoukas, and Theodorou (Michail *et al.*, 1957), but the syndrome was named after Rubinstein and Taybi, who described 7 patients (Rubinstein and Taybi, 1963). Since then, a number of cases of individuals with RTS have been reported. Also, several cases accompanying neoplasms have been reported and the association between them has been considered (Russell *et al.*, 1971; Jonas *et al.*, 1978; Sobel *et al.*, 1981).

Here we describe a case of medulloblastoma associated with RTS.

CASE REPORT

An 8 1/2-year-old girl with RTS was admitted to Seoul National University Children's Hospital because of irritability for one month.

She was delivered at term by Caesarean section due to placenta previa and had a birth weight of 2.3 kg. The anterior fontanelle was large. She had suffered from recurrent respiratory infections, otitis media, and feeding difficulties in infancy. At 2 1/2 years old, she started to sit alone. At 3 years old, a ligation of patent ductus arteriosus and an operation on the entropion were performed without complication. She started to walk alone from 5 years old. She could speak a few words such as "mama" and "papa" at 7 years old.

On admission, she looked dull and irritable with profound mental retardation. Height was 120 cm and head circumference was 49 cm; both measurements were 3 S.D. below normal, while her weight was 32 kg (50th percentile). Her blood pressure was 110/70 mmHg, heart rate 52 per minute, respiration rate 16 per minute, and body temperature 36.8℃. This child had a shaggy, prominent forehead, long eyelashes, thick and high-arched eyebrows, strabismus, epicanthal folds, downward

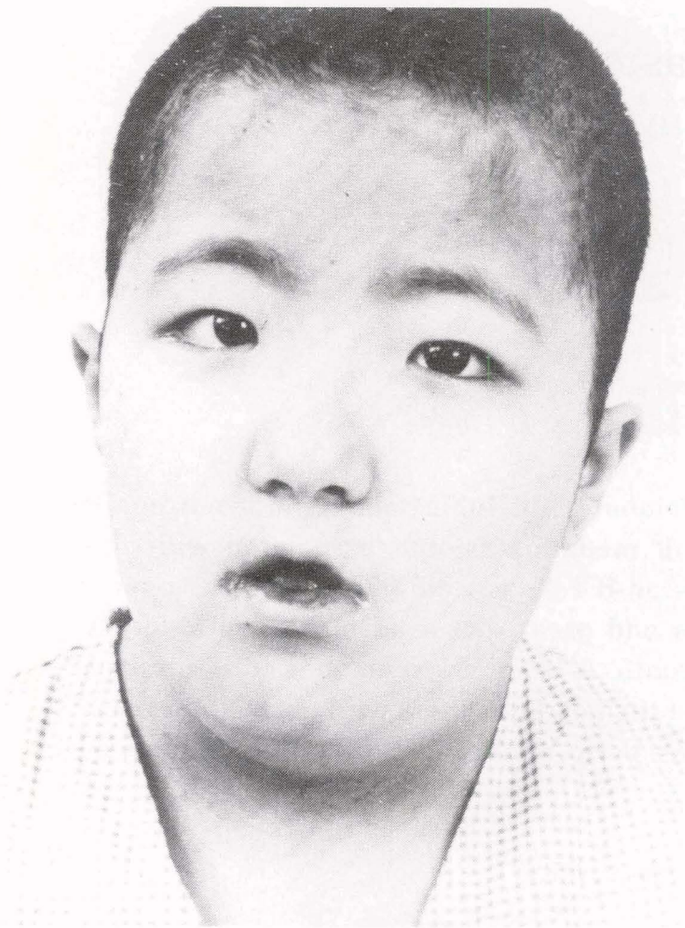

Fig. 1. Gross facial appearance showed a shaggy, prominent forehead, long eyelashes, thick and high-arched eyebrows, strabismus, epicanthal folds, downward slanting of palpebral fissures, hypoplastic midface, micrognathia, and a broad-based nose.

slanting palpebral fissures, hypoplastic maxilla, high-arched palate, and micrognathia with mild retrognathia. Her nose was broad-based, the septum extending below the alae (Fig. 1). Distal phalanges of all the fingers and toes appeared widened with marked broadening and partial syndactyly of the thumbs and great toes (Fig. 2). She had right dorsal scoliosis, a funnel chest, and hypertricosis. On neurologic examination, her consciousness was clear. Light reflex was barely noticeable with mydriasis, while the other cranial nerve examination was unremarkable. The motor strength was within normal range, but the muscle tone of all the extremities was increased. The full assessment of the sensory system could not be made due to profound mental retardation. Deep tendon reflexes were increased, and Babinski reflex was present bilaterally. Her gait was wide-based, but finger-to-nose test and rapid alternating movements were normal.

A brain CT scan showed a homogeneously enhanced round mass in the midline of the posterior fossa with marked hydrocephalus (Fig. 3). Electroencephalography showed a moderate abnormal waking record due to excessive slowness of the posterior rhythm of mainly theta frequency activity. A chromosomal study was normal. Her bone age was that of a 7 11/12-year-old. The acetabular angle was 8 degrees on the left side and 5 degrees on the right.

Extraventricular drainage was carried out in the right frontal area because of signs of impending herniation of the brain. A midline suboccipital craniotomy with a C_1 laminectomy were performed with gross total removal of the mass. Whole spine myelography and cytospin showed negative findings. Pathologic examination of the mass showed findings of medulloblastoma with desmoplastic type (Fig. 4). Craniospinal irradiation was started 4 weeks after the completion of operation. The whole brain received 3,600 cGy in 24 fractions over a 5-week period with a subsequent boost to the fourth ventricle area to a final tumor dose of 5,580 cGy in 35 fractions over 52 days. Spinal irradiation (2,400 dose in 20 fractions over 29 days) completed the treatment. Currently, 14 months after the operation the patient is still clinically free of any disease and is attending a school for the retarded.

DISCUSSION

Since 1963, when Rubinstein and Taybi first reported 7 cases of the syndrome that now bears their names, there have been hundreds of reported cases of Rubinstein-Taybi syndrome. Despite its wide recognition, RTS still lacks a pathognomonic requirement. The spectrum of findings judged to have the greatest diagnostic importance includes broad great toes and thumbs and sometimes other fingers, moderate-to-severe mental and motor retardation, short stature, retarded bone age, microcephaly, beaked or straight nose with the septum extending below the alae and a broad nasal bridge, ear anomalies, mild retrognathia, high-arched palate, peculiar grimacing smile, apparent hyper-

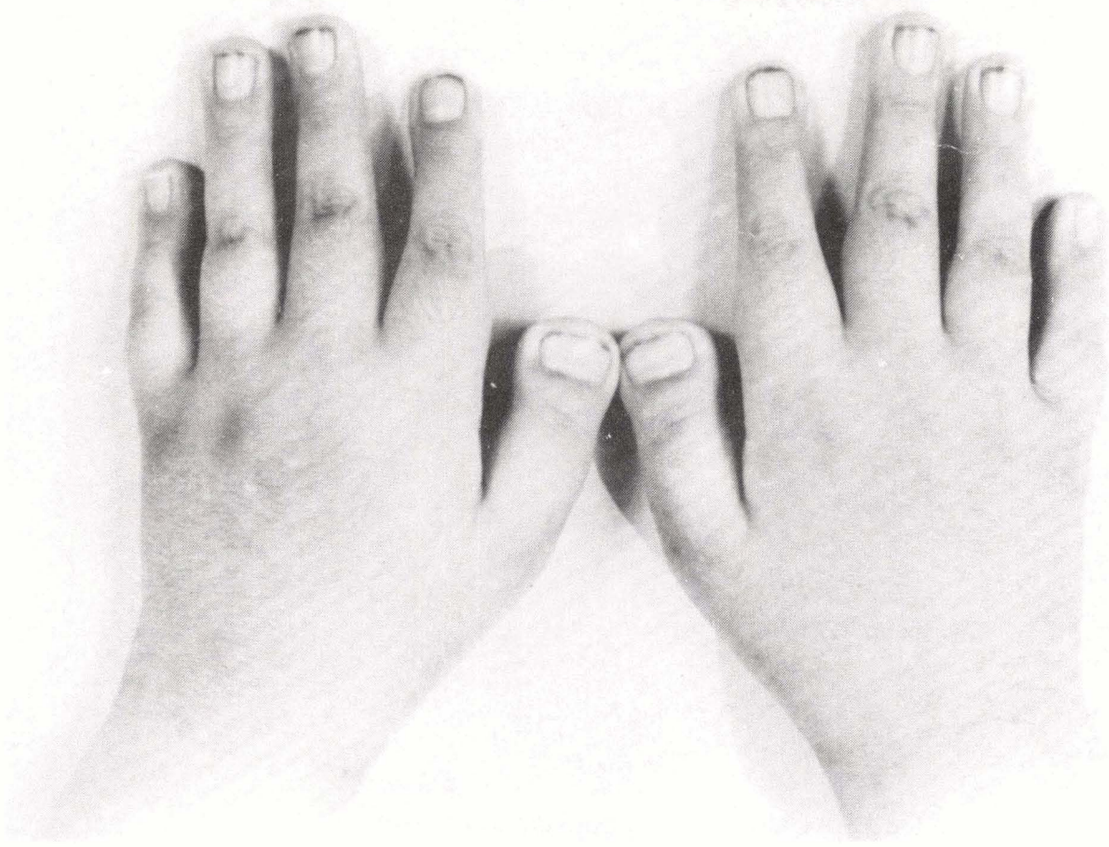

Fig. 2. Gross appearance of both hands showed a marked broadening of thumbs and some widening of the distal phalanges of the other fingers.

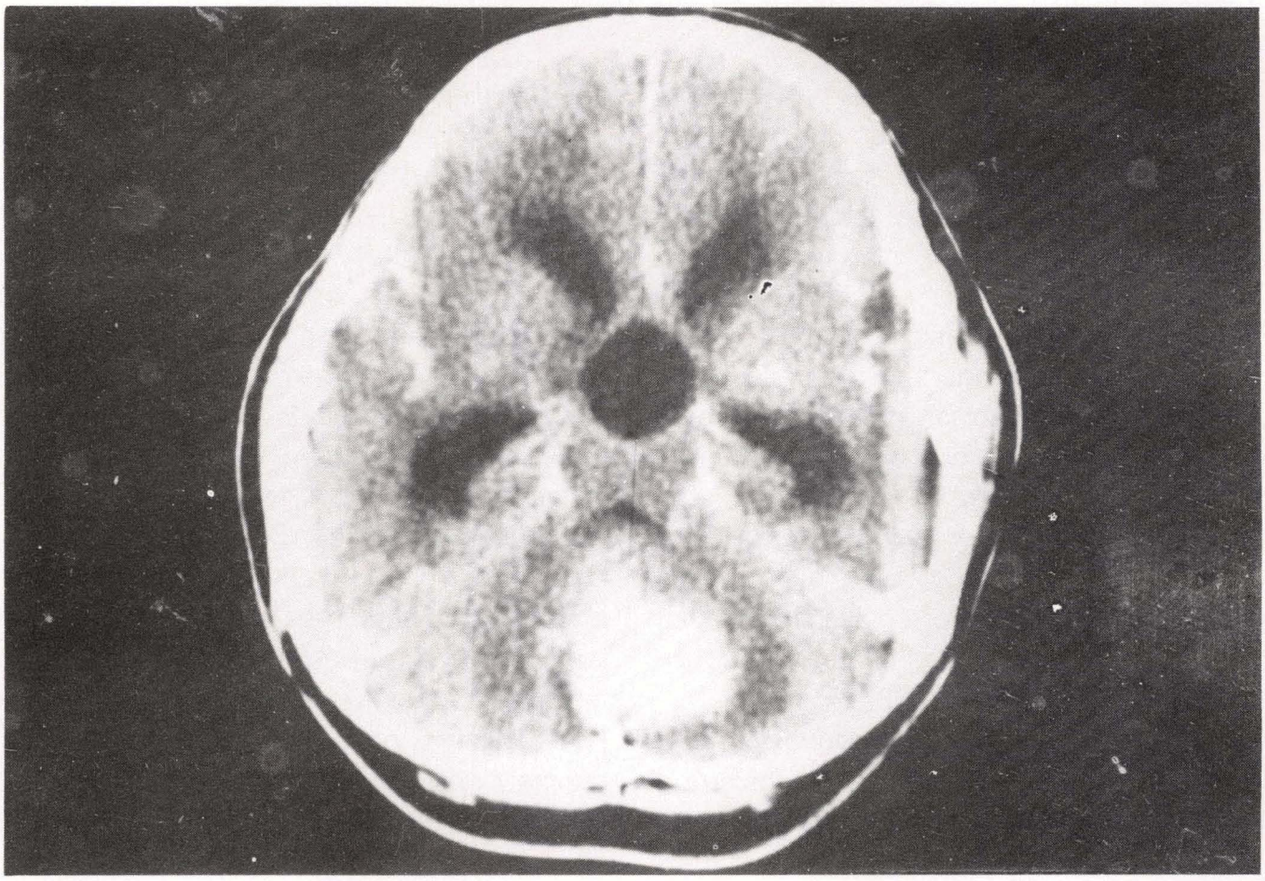

Fig. 3. A brain CT scan showed a homogeneously enhanced round mass lesion in the midline of the posterior fossa with marked hydrocephalus.

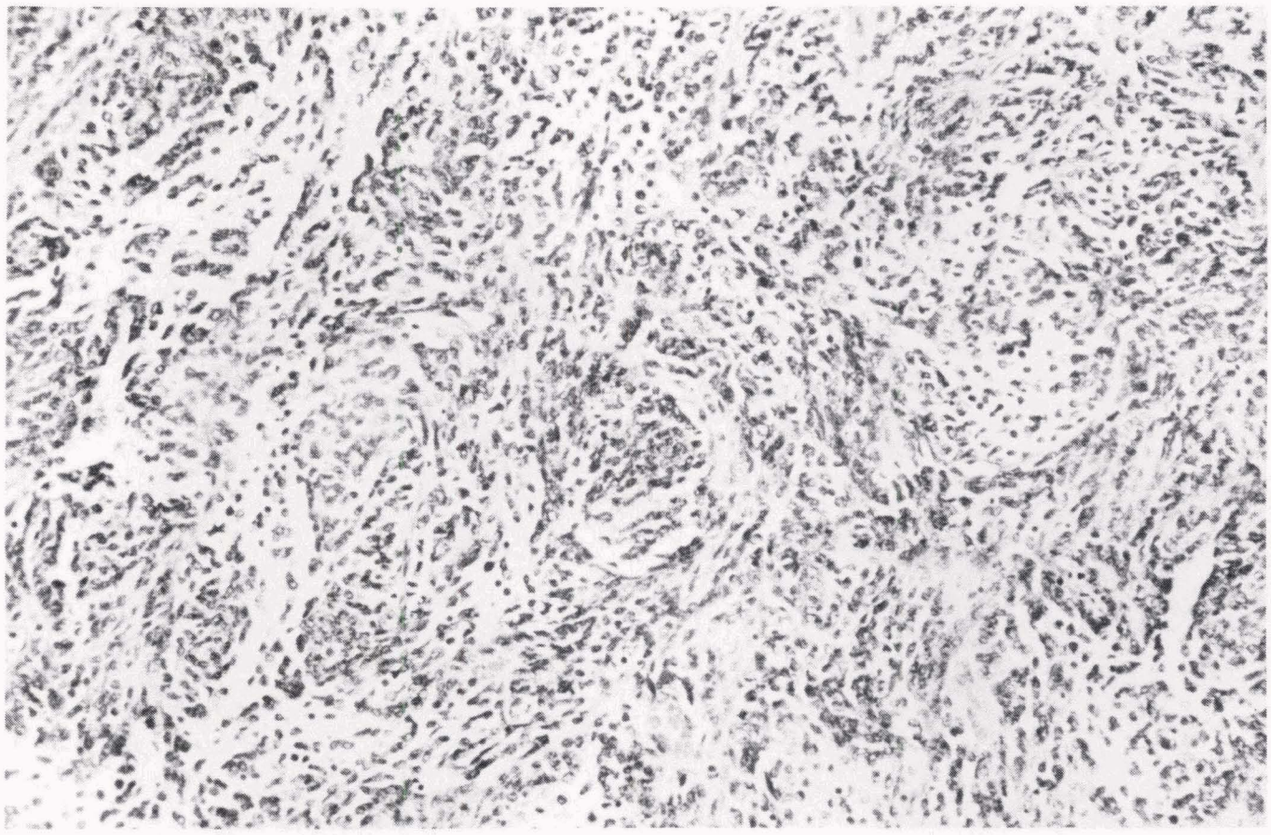

Fig. 4. Photomicrograph of the medulloblastoma. In the background of high cellularity of the tumor mass there are irregular fine strands of fibrous tissue, showing streaming appearance. There are also islands of dark smaller cells in the fibrillary background. This type of tumor is called desmoplastic medulloblastoma (H & E × 100).

telorism, anti-mongoloid slant of the palpebral fissure, strabismus, EEG abnormalities, stiff, awkward, and unsteady gait, incomplete descent of the testes, neonatal distress or recurrent respiratory infections, and feeding difficulties in infancy (Rubinstein and Taybi, 1963; Jones, 1988).

This case had many physical stigmata of the above characteristic findings and the patient was easily diagnosed as Rubinstein-Taybi syndrome when she was 4 months old. On this admission, the diagnosis of the medulloblastoma was not clinically apparent because she could not verbally complain of her symptoms due to profound mental retardation. Another source of confusion was that several authors have described pyramidal tract signs in RTS (Padfield *et al.*, 1968).

The relationship of congenital malformation and childhood neoplasm gained impetus with the report of Wilms' tumor occurring in association with sporadic aniridia or contralateral hemihypertrophy (Miller *et al.*, 1964). In RTS, several cases combining with the neoplasm, such as acute leukemia, intraspinal neurilemmoma and rhabdomyosarcoma, have been reported (Russell *et al.*, 1971; Jonas *et al.*, 1978; Sobel *et al.*, 1981). These reports suggest that RTS-neoplasm association remains fairly strong. Siraganian *et al.* (1989) reports that 19 patients had 22 tumors among the 574 individuals with RTS, and the risk of acute lymphocytic leukemia in childhood among them is as high as that of Down syndrome (Jonas *et al.*, 1978; Siraganian *et al.*, 1989). In other words, RTS may be predisposed to leukemia as it does to Down syndrome. Down syndrome, Fanconi syndrome, and ataxia telangiectasia are prone to have leukemia, and they have chromosomal anomalies or immunologic abnormalities, so it can be postulated that RTS might have the above abnormalities. In fact, several cases of RTS with immunologic abnormality or chromosomal anomaly were reported (Jonas *et al.*, 1978; Hennekam *et al.*, 1989), but no firm conclusion as to the cause of RTS can be made from these figures. To our knowledge, this is the first reported case of medulloblastoma associated with this syn-

drome. In this case, a chromosomal study was normal and an immunologic study was not done because the patient's parents refused permission.

Until now, it is not known which defect leads to an increase in neoplasms in RTS, but perhaps genetically-induced developmental errors that lead to RTS may possibly also lead to other certain neoplasms. The knowledge of the relationship between them will help us to discover the cause , prevention, and treatment of RTS.

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=국 문 초 록=

Rubinstein-Taybi 증후군에 동반된 수아세포종 1례

서울대학교 의과대학 소아과학교실, 신경외과학교실* 및 병리학교실**

장영진 · 황세희 · 황용승 · 조병규* · 지제근**

Rubinstein-Taybi 증후군은 특징적인 얼굴 모양, 정신 박약 및 넓은 모지와 족지가 특징인 선천적 기형이다. 이 증후군과 여러 기관의 종양이 동반된 예가 보고된 바 있으나, 중추신경계 종양으로 수아 세포종이 동반된 증례의 보고는 저자들이 아는 한 아직 없었다. 저자들은 8년 5개월된 Rubinstein-Taybi 증후군 환아에서 수아 세포종으로 진단된 1례를 경험하였기에 문헌고찰과 함께 보고하는 바이다.