J Korean Med Sci 2001; 16: 245-9
ISSN 1011-8934

Multiple Intracranial Aneurysms Associated with Branchio-Oto-Dysplasia

Branchio-oto-dysplasia is characterized by abnormalities of embryonic branchial arch system and deafness inherited as autosomal dominant with variable gene expression. We present a rare case of multiple intracranial aneurysms associated with branchio-oto-dysplasia. A 40-yr-old man with severe headache presented as spontaneous subarachnoid hemorrhage on brain computed tomographic scan. The patient also manifested clinical features of branchio-oto-dysplasia and right hemifacial hypoplasia. Carotid angiogram confirmed an aneurysm in the anterior communicating artery. Intraoperative findings demonstrated multiple aneurysms in the anterior communicating artery and in the left posterior communicating artery, which were clipped successfully. Postoperative course was uneventful. This condition has not been reported previously. We also reviewed literatures to discuss whether the intracranial aneurysm was as a coincidental finding or a part of this malformation.

Key Words: *Branchio-Oto-Renal Syndrome; Intracranial Aneurysm; Subarachnoid Hemorrhage*

Jin Hwan Cheong, Choong Hyun Kim, Koang Hum Bak, Jae Min Kim, Suck Jun Oh

Department of Neurosurgery, Hanyang University Kuri Hospital, Hanyang University College of Medicine, Kuri, Korea

Received: 22 May 2000
Accepted: 7 July 2000

Address for correspondence
Choong Hyun Kim, M.D.
Department of Neurosurgery, Hanyang University Kuri Hospital, 249-1 Kyomun-dong, Kuri 471-701, Korea
Tel: +82.31-560-2322, Fax: +82.31-560-2327
E-mail: KCH5142@email.hanyang.ac.kr.

INTRODUCTION

Many investigators have been interested in the genetic risk factors or genetic syndromes which may be connected to the development of intracranial aneurysms. And the reports on the association of intracranial aneurysms with numerous heritable connective tissue disorders are increasing (1-4).

Branchio-oto-dysplasia, often called as BO syndrome, is a relatively uncommon malformation associated with dysmorphogenesis of the first and second branchial arches (2). It is an autosomal dominant disorder (5, 6) which was first described by Melnick et al. in 1976 (7). The major features of this entity consist of hemifacial microsomia, which is thought to result from vascular injury of stapedial artery (8, 9), congenital microtia, auditory meatal atresia and hearing loss (10). The association of BO syndrome and intracranial aneurysms has not been documented previously. We report a patient who had BO syndrome and multiple intracranial aneurysms and was treated with surgical clipping. In this report, we present a review of literatures to elaborate upon hypothesis whether intracranial aneurysms relate to BO syudrome as a coincidental finding or as a part of this malformation.

CASE REPORT

A 40-yr-old man with lethargic mentality was admitted to the hospital following a sudden onset of a severe headache, nausea, and vomiting. His family history was not contributory. Physical examinations showed a right rudimentary auricle, right facial nerve palsy, and hypoplasia, and absence of the right external auditory meatus (Fig. 1).

The patient also showed bifid uvula. Temporal bone computed tomographic (CT) scans revealed the complete lack of right external auditory canal, middle ear, ossicles, and a normal inner ear (Fig. 2). There were no abnormalities in the left ear. Abdominal ultrasonography showed normal kidneys. A brain CT scans revealed hyperdense lesions in both Sylvian cisterns and basal cistern that were consistent with acute subarachnoid hemorrhage (Fig. 3). Cerebral angiography demonstrated an aneurysm in the anterior communicating artery (ACoA) (Fig. 4A-B). Immediately after the stroke, a right fronto-temporal craniotomy was performed. Intraoperative findings demonstrated multiple aneurysms in the ACoA and the left posterior communicating artery (PCoA). The aneurysm of ACoA was round with the base of the lesion measuring 8mm and the apex protruding

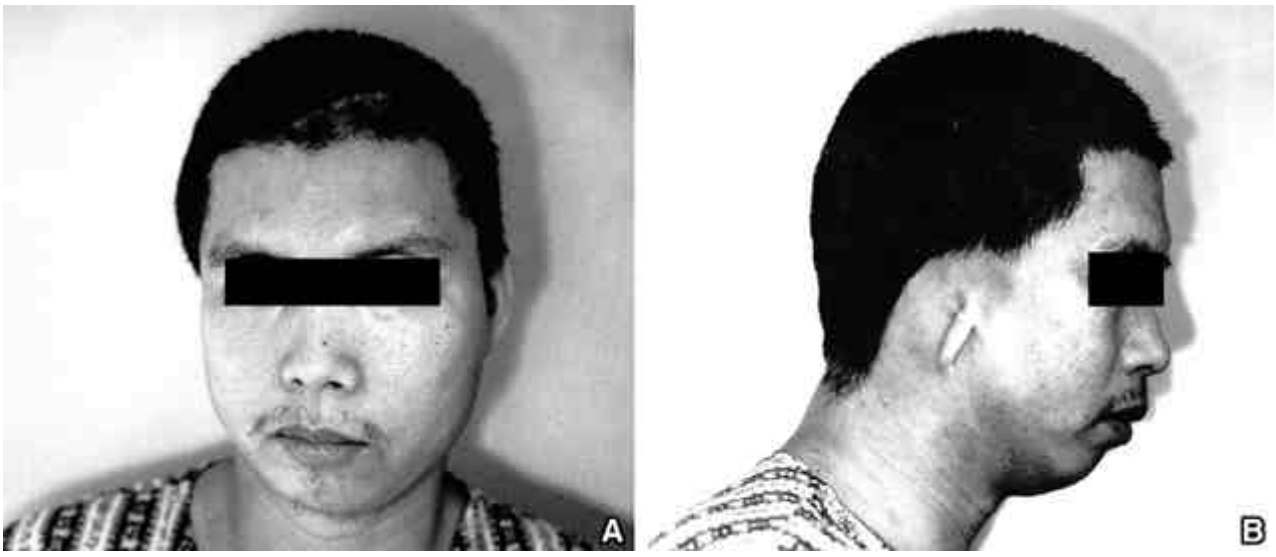

Fig. 1. Photographs of the patient showing hemifacial microsomia, facial nerve palsy, and auditory meatal atresia of the right side.

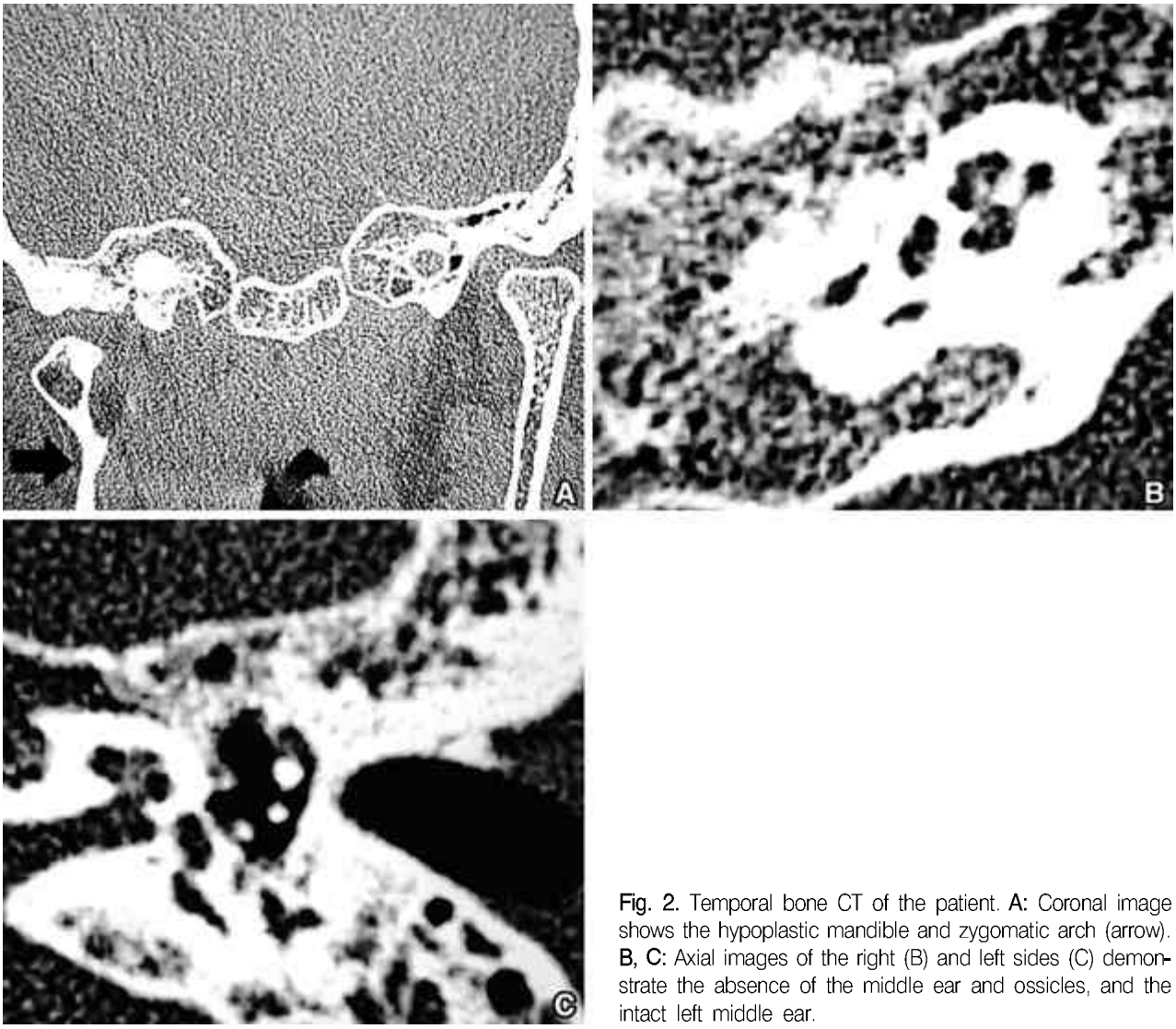

Fig. 2. Temporal bone CT of the patient. **A:** Coronal image shows the hypoplastic mandible and zygomatic arch (arrow). **B, C:** Axial images of the right (B) and left sides (C) demonstrate the absence of the middle ear and ossicles, and the intact left middle ear.

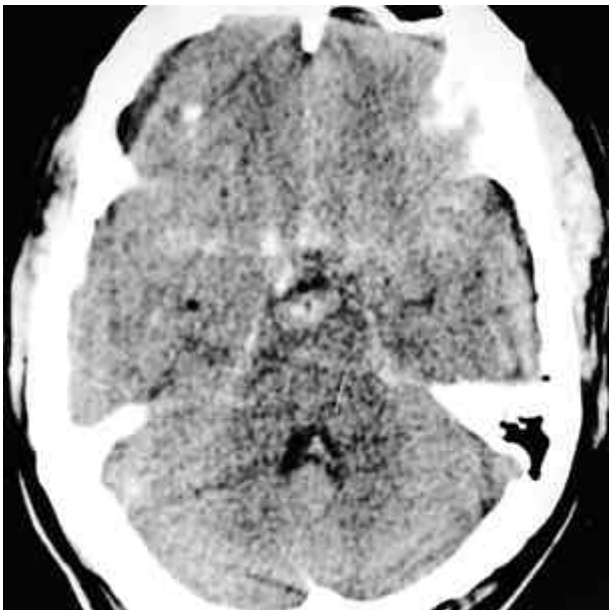

Fig. 3. Brain CT scan shows subarachnoid hemorrhage in both Sylvian and basal cisterns.

into the right frontal lobe. The contralateral left anterior cerebral artery (ACA) was hypoplastic. The aneurysm of PcoA, which was 5 mm in size, was found in the origin of PcoA, and was clipped successfully (Fig. 4C-D). He made an uneventful postoperative recovery.

DISCUSSION

Etiology and pathogenesis of intracranial aneurysms are multifactorial, with genetic factors or possibly genetic syndromes playing an increasingly recognized role (3, 11, 12). The association of various heritable disorders with intracranial aneurysms and the familial aggregation of intracranial aneurysms in the absence of any known systemic disorders suggest that the genetic factors also play a role in the cause and pathogenesis of intracranial aneurysms (10). Intracranial aneurysms have been associated with numerous heritable connective tissue disorders, which account for at least 5% of the cases. Of various heritable disorders that have been associated with intracranial aneurysms, the most important diseases are Ehler-Danlos syndrome type IV, Marfan's syndrome, neurofibromatosis type I, autosomal dominant polycystic kidney disease, and α-1-antitrypsin deficiency fibromuscular dysplasia (1, 3, 11, 13, 14). Although the benefits have never been quantified, screening for the asymptomatic intracranial aneurysms should be considered in patients who are suspected of generalized connective tissue disorder.

The association of branchial arch anomalies, hearing loss, and renal anomalies was first described by Melnick et al. in 1976 (7) and is termed branchio-oto-renal syndrome. Embryologically, this condition is due to the defective development of the first and second branchial arch structures (9). It is an autosomal dominant condition with variable expression in gene carrier (5, 15, 16). The branchio-oto-renal syndrome (BOR syndrome) gene lies on chromosome 8 (8 q, 13.3), and several research laboratories offer molecular genetic testing for the affected families (10, 17). Patients with BO syndrome typically present mild to severe hearing impairment. It may be sensorineural (20%), conductive (30%), or mixed (50%), and the type of hearing loss may differ between two ears. Preauricular pits may be present, and most frequently observed auricular deformities are cup ears (4, 6, 10, 17, 18). Renal anomalies such as polycystic, hypoplastic, or totally absent kidneys are common (19). These cardinal signs can be accompanied by stenosis of the lacrimal ducts (4, 15), facial nerve paralysis and vestibular anomalies.

In our case, physical examinations and neuroimaging studies showed malformations in the first and second branchial arch system. In addition, right facial nerve paralysis and facial hypoplasia were accompanied, but the kidney was not compromised. BO syndrome has been described as a distinct entity, but it is now thought to be one spectrum of the BOR syndrome, with oto-renal (OR) syndrome, in which only otologic and renal involvement is seen, possibly representing other end of the spectrum (BO-BOR-OR) in the BOR syndrome (7, 10, 17). Therefore, the malformations of the BO syndrome compromise several organs that are apparently unrelated to each other spatially and embryologically (5). From the literatures, it is concluded that the simultaneous affection of the ear, the branchial and other systems may be caused by the effect of a single gene on a mechanism controlling the differentiation of these organs. These suggest some ultrastructural similarities, which could involve common surface recognition proteins or enzymatic receptors (5, 16, 19). Animal experiments that have demonstrated the immunologic similarities between cochlea and kidney tend to support this hypothesis, and these data must be applied to the human embryo but only with caution (16). Such similarity appears to be particularly strong between the stria vascularis of the ear and the renal glomeruli (18). Autopsy study with the BOR syndrome demonstrated that the stria vascularis was dysplastic and atrophic, and that the cochlear cavity was hypoplastic with a reduced number of cochlear neurons (19). Histologically, both abrupt interruption and partial disappearance of internal elastic lamina are found frequently in the wall of Willis's circle. This abnormality of internal elastic lamina may be attributable to con-

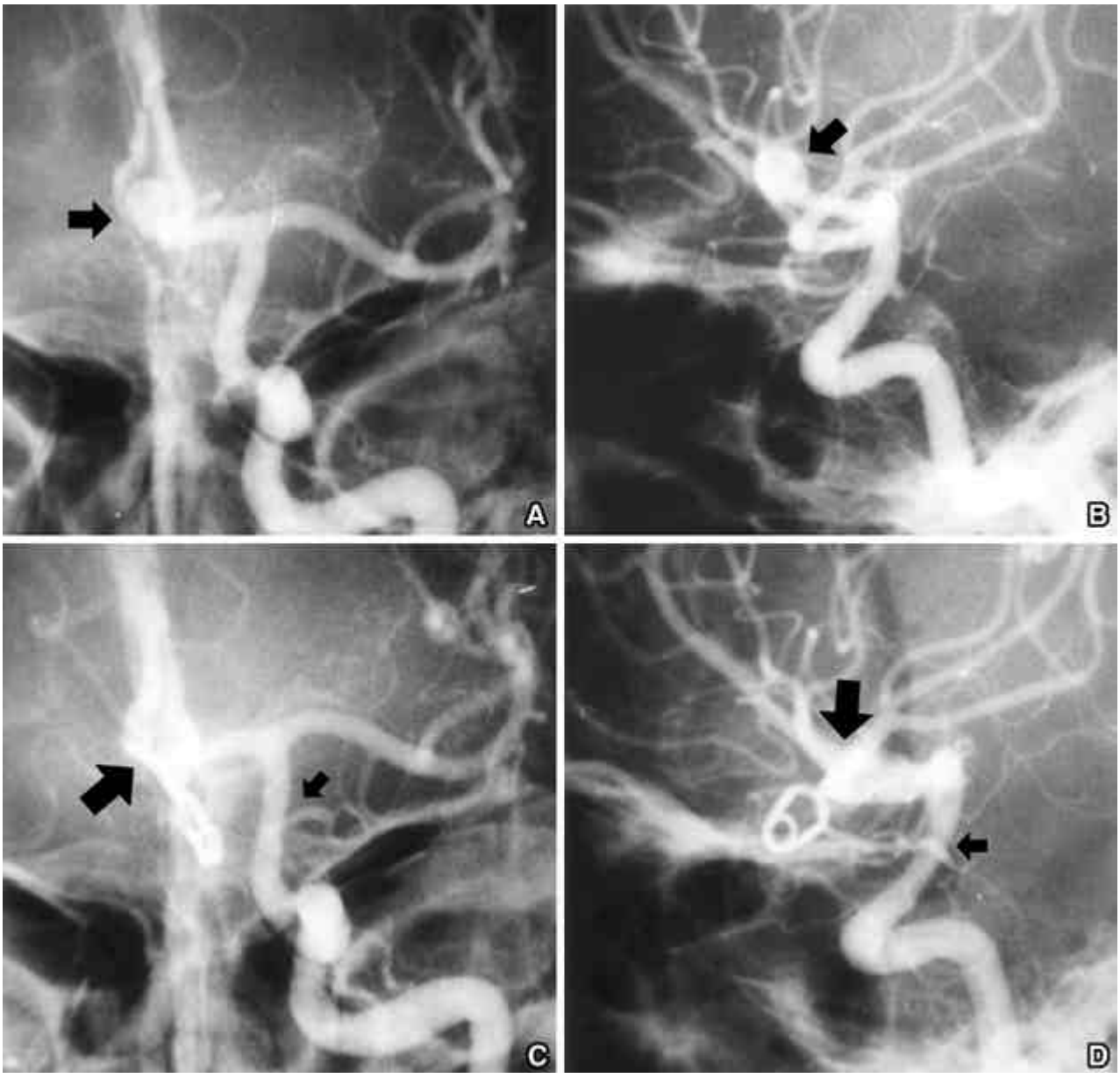

Fig. 4. Left carotid angiograms obtained in the patient. **A, B:** Preoperative images demonstrate an aneurysm in the anterior communicating artery (arrow) which projected superiorly (A: anteroposterior view, B: lateral view). **C, D:** Postoperative angiograms demonstrate successful clipping of the aneurysms in the anterior communicating artery (large arrow) and posterior communicating artery (small arrow) (C: anteroposterior view, D: lateral view).

genital factors and increase the frequency of the occurrence of intracranial aneurysms in inherited kidney disease (20).

In conclusion, the report attempts to provide some clue to the question the correlation between multiple intracranial aneurysms and BO syndrome by reviewing the related literatures. The correlation between BO syndrome and multiple intracranial aneurysms is poorly established at present, we suggest that further study is necessary to determine whether intracranial aneurysms are coincidental findings or whether they represent de novo aneurysm formation.

REFERENCES

1. Lan MY, Liu JS, Chang YY, Lin SH, Chen WH, Chen SS. *Fibromuscular dysplasia associated with intracranial giant aneurysm: report of a case. J Formos Med Assoc 1995; 94: 692-4.*
2. Lida H, Naito T, Hondo H, Demachi H, Aoki S. *Intracranial aneurysms in autosomal dominant polycystic kidney disease*

detected by MR angiography: screening and treatment. Nippon Jinzo Gakkai Shi 1998; 40: 42-7.

3. Schievink W. *Genetics of intracranial aneurysms. Neurosurgery 1997; 40: 651-62.*
4. Schievink WI, Puumala MR, Meyer FB, Raffel C, Katzmann JA, Parisi JE. *Giant intracranial aneurysm and fibromuscular dysplasia in an adolescent with α-1-antitrypsin deficiency. J Neurosurg 1996; 85: 503-6.*
5. Fraser FC, Ling D, Clogg D, Nogrady B. *Genetic aspects of the BOR syndrome. Am J Med Genet 1978; 2: 241-52.*
6. Gimsing S, Dyrmose J. *Branchio-oto-renal dysplasia in three families. Ann Otol Rhinol Laryngol 1986; 95: 421-6.*
7. Melnick M, Hodes ME, Yune H, Nanc WE, Sweeney A. *Branchio-oto-renal dysplasia and Branchio-oto-dysplasia: two distinct autosomal dominant disorders. Clin Genet 1978; 13: 425-42.*
8. Allen WE, Kier EL, Rothman SL. *The maxillary artery: normal arteriographic anatomy. Am J Roentgenol Radium Ther Nucl Med 1973; 118: 517-27.*
9. Daseler EH, Anson BJ. *Surgical anatomy of the subclavian artery and its branches. Surg Gynecol Obstet 1959; 108: 149.*
10. Shievink W, Schaid DJ, Rogers HM, Piepgras DG, Michels VV. *On the inheritance of intracranial aneurysms. Stroke 1994; 25: 2028-37.*
11. Gokalp HZ, Avman N, Ozkal E, Gokben B. *Brain tumor associated with intracranial arterial aneurysm. Acta Neurochir (Wien) 1980; 53: 267-73.*
12. Momma F, Beck H, Miyamoto T, Nagao S. *Intracranial aneurysm due to metastatic choriocarcinoma. Surg Neurol 1986; 25: 74-6.*
13. Buge A, Vincent D, Rancurel G, Dechy H, Dorra M, Betourne C. *Behcet's disease with multiple intracranial arterial aneurysms. Rev Neurol (Paris) 1987; 143: 832-5.*
14. Jourdan C, Lamy B, Artru F, Convert J, Mottolese C, Poirot I, Tixier S, Terrier A, Chiaara Y, Lamy B. *Intracranial aneurysm and dysplasia of elastic tissue: pre- and postoperative problems. Agressologie 1990; 31: 405-8.*
15. Gutierrez C, Bardaji C, Bento L, Martinez MA, Conde J. *Branchio-oto-renal syndrome: incidence in three generations of a family. J Pediatric Surg 1993; 28: 1527-9.*
16. Quick CA, Fish A, Brown C. *The relationship between cochlea and kidney. Laryngoscope 1973; 83: 1469-82.*
17. Gupta A, Patton MA. *Familial microtia with meatal atresia and conductive deafness in five generations. Am J Med Genet 1995; 59: 238-41.*
18. Melnick M, Myrianthopoulos NC, Paul NW. *External ear malformations: epidemiology, genetics, and natural history. Birth Defects Orig Artic Ser 1979; 15: i-ix, 1-140.*
19. Fitch N, Srolovitz H. *Severe renal dysgenesis produced by a dominant gene. Am J Dis Child 1976; 130: 1356-7.*
20. Ikeda H, Yoshimoto T. *Pathological study of Willis's circle in autopsy cases of polycystic kidney disease. No To Shinkei 1987; 39: 909-13.*