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Neuroanatomic Study on Holoprosencephaly

전종뇌의 신경해부학적 검색

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INTRODUCTION

In 1882 Kundrat grouped a number of cerebral malformation under the designation of arhinencephaly. In 1959, Yakovlev carefully studied 10 cases and pointed out that the term arhinencephaly was a misnomer because parts of rhinenceph alon were present. Subsequently, the term holoprosencephaly has come into use for this brain deformity.

In the past years, a number of reports have appeared, pointing out the relationship between the facial and cerebral manifestations, (DeMyer et al., 1963: DeMyer et al., 1964) familial occurrence, (DeMyer et al., 1963: Hintz et al., 1968) endocrine dysgenesia, (Edmonds, 1950; Haworth et al., 1961; Hintz et al., 1968) chromosomal abnormalities, (Gorlin et al., 1968; Lorch et al., 1978) bony change, (Siebert et al., 1981) radiologic, (Kulander et al., 1966) echoencephalographic (Patel et al., 1980) and computerized tomographic changes (Derakhsh et al., 1980). In this report, we are concerned about the relationship between the facial and cerebral manifestations and the certainty of the anterior-posterior gradient. We also laid emphasis on the changes of the pituitary gland and cerebellum. And on the basis of our observations, we reconsidered the pathogenesis of the holoprosencephaly which has so far been presented.

MATERIALS

A total of 11 cases could be collected at the Department of Pathology, Seoul National University Hospital during a period of 6 years from 1976 to 1982.

All these cases were from the file of Registry of Congenital Malformation of Seoul National University, except for one case from Korea University Hospital (Dr. I.S.Kim), one case from Paik Foundation Hospital (Dr. I.H.Koh), and one case from Eul-ji Hospital (Dr. Y.H. Park). These materials are summarized in Table 1.

Pre- and postnatal clinical informations were not available in full detail in most cases. The specimens were examined at the Department of Pathology of Seoul National University.

Routine procedures of postmortem examination were done. The brains were removed and fixed in 10% formalin for 2 weeks before it were cut coronally. Sections for microscopic examinations were made and stained with hematoxylin-eosin, cresyl violet and luxol fast blue.

OBSERVATIONS

Our cases showed obvious female preponderence. Among 11 cases 8 cases were female and

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3 cases were male. Case XI survived for 15 days but the majority was stillbirth or died within 1 day (Table 1). Gestational age was 32 weeks in case IV; 33 weeks in II and III and 34 weeks in I. Other cases were of full term delivery. Head circumference was 54 cm in case VIII, 42.5cm in VI, 36cm in IX and 33cm in I and X. Other cases ranged from 24 to 30cm. In case IV, heart anomalies, such as atrial septal defect, ventricular septal defect and coarctation of aorta were identified. Internal examination of case V showed situs inversus totalis. In case VII, polydactyly, rockerbottom feet, tetralogy of Fallot, bicornuate uterus and intrasplenic pancreatic tissue were noted. Examination of the hands in case IX showed shortness of the right 3rd and 4th fingers and simian crease of the left hand.

Prosoporhinal malformation included a variety of anomalies which were listed in table 1. The sequence of the cases was arranged according to the estimated severity of the prosoporhinal malformation. Eye: Cyclopia was seen in 4 cases, hypotelorism in 4, hypertelorism in 1 and normal in 2. Morphology of the cyclopia was also variable. Case I and II disclosed bulging out of the eyeball but other two were present in the orbital cavity. In case I, the both eyes had one cornea, one sclera and fused pupil (Fig. IA). Other cases showed complete fusion.

Examination of the eyeballs in 6 cases revealed that 5 cases (cases I, II, III, IV and VII) had coloboma of iris, and one case (case V) had conjunctival coloboma (Fig. 2) The optic nerves and chiasm were malformed in 4 cyclopias but others were normal. Case I showed thin optic nerves (Fig. 1B). In case II the optic chiasm and the left optic tract were absent and the right optic nerve was hypoplastic. The optic nerves in case III and IV were represented by only one optic trunk.

Nose: The nose was absent without proboscis in cases II, VII and IX and, was represented by the proboscis in cases I and IV. Case V and VI had one nostril each (cebocephaly). The nostril in case VI was connected to the nasal cavity but, in case V, it ended blindly. In case III, above the single eye, a huge proboscis-like mass was protruded from the forehead (Fig. 4B). Case VIII, X and XI had the normal nose with two nostrils.

Lip: The lip was normal in 7 cases. In cases I and II, oral cavity was not seen. Instead, in case I, a protruding irregular shaped mass, measuring 4.5cm in length and 2.0cm in width, was noted above the proboscis. Section from this protruded mass revealed stratified squamous epithelium and a variety of structures, such as salivary glands, skeletal muscles, tooth, tonsil, bony structures and ectopic thyroid. Case V showed that the extremely small mouth, measuring 0.4cm, ended blindly (Fig. 2). Bilateral cleft lip was noted in case VII.

Ear: Both ears in case I and II were medially fused (synotia) and ear canals were atretic (Fig. 1A). In case V. two ear lobes were closely approximated in their developmental horizon (juxtaotia) (Fig. 2). The left ear canal was patent but the right one was atretic. Agnathia was also noted in these 3 cases. Ears were low set in all cases.

Relationship between the prosoporhinal and cerebral malformation: Among the 4 cases of cyclopia, 3 cases showed alobar holoprosencephaly as cerebral malformation but characteristically case I did not (Fig. 1C). Cebocephaly was seen in 2 cases. Case VI had alobar type and case V showed semilobar type (Fig. 2). Face with bilateral cleft lip was associated with semilobar type in case VII and, in case VIII, only hypotelorism was accompanied with the alobar type. Case IX, which had hypertelorism and arhinia, showed alobar type (Fig. 3), while in cases X and XI, normal face

Table 1. Prosoporhinal malformation in relationship with the type of holoprosencephaly

Case No.	Age(day)	Sex	Eye	Nose	Lip	Type of holoprosen.
I	SB	F	cyclopia	proboscis	N	lobar(?)
II	—	〃	cyclopia	arhinia	〃	alobar
III	1	〃	cyclopia	arhinia	absent	alobar
IV	SB	〃	cyclopia	proboscis	malformed	alobar
V	1	M	hypotel.	1 nostril	fish-like	semi-lobar
VI	SB	—	hypotel.	1 nostril	N	alobar
VII	SB	F	hypotel.	arhinia	bilat. cleft	semi-lobar
VIII	SB	〃	hypotel	N	N	alobar
IX	0.5	〃	hypertel.	arhinia	N	alobar
X	0.5	M	N	N	〃	alobar
XI	15	〃	〃	〃	〃	unclassified

SB; Still Birth N; Normal

was associated to the holoprosencephaly, and was of alobar type in case X. (Fig. 4).

Cases II, III, IV VIII, IX showed complete absence of the interhemispheric fissure. The cerebrum was unpaired and consisted of a large single dorsal cyst. Neither olfactory tracts and bulbs nor corpus callosum was present. In the floor of the single cavity, the corpora striata and the thalami were fused in the midline except for case IX, in which the corpora striata were separated. In case VIII, the cerebrum appeared to be rectangular shape (11×13.5cm) and hydrocephalic. Anterior view of the cerebrum showed that a small defect was present at the left temporal lobe without communication with the cavity and small blood vessels were abnormally proliferated at the ventral and superior aspect of the defect and the contralateral site in the right lobe. Sections from area adjacent to this defect showed micropolygyria. Heterotopic pineal body was found at the left end of the transverse convolution. Associated with this heterotopia of the pineal body, thalami, midbrain and pons appeared to be displaced to the right. The subependymal vein, which was a midline structure in other cases, was on the left corpus striatum and appeared to be elongated. Case III, which was also classified as alobar type, showed unusual features. The cerebrum did not have dorsal cyst and the interhemispheric fissure was rudimentarily present through its entire length. Coronal sections of the brain disclosed obliteration of the single cavity (Fig. 5C,D).

Characteristically this obliterated single ventricle did not connect with the third ventricle nor have the opening. Associated with this abnormality of the ventricular system, location of the thalami was also unusual. They were found behind the holosphere and appeared not to be related with the single cavity. Only a part of diencephalon was connected to the occipital portion of the cerebrum. Between the thalami, a pit of the third ventricle was opened to the supdural space(Fig. 5E).

In case V and VII, the interhemispheric fisssure was absent anteriorly. Posteriorly, a deep, convoluted median fold of the cortical plate formed a blind pocket between rudimentary occipital lobes.

Sectioning of the anterior portion of the cerebrum showed a large unpaired ventricle crowning the striatal eminence. Posteriorly, this made its posterior-lateral outpocketings to two paired

hemispheres. Corpus callosum was rudimentarily present. Examination of the case XI disclosed very unusual features. Two hemispheres were asymmetric, bulkier on the right side. The interhemispheric fissure was present in frontal and occipital portions, but middle half showed the fusion of the two hemispheres (Fig. 5B). Gyral pattern was unorganized and depth of the sulci was varied from shallow cleft to extremely deep fissure. Hypoplasia of the frontal lobe was not seen. Olfactory tracts were identified in the olfactory sulcus, but having been torn, olfactory bulbus were not seen (Fig. 5C). Coronal sections of the brain disclosed the abnormal changes of the ventricle (Fig. 5D,F). In front of the temporal lobe (lst cut), where the interhemispheric fissure was present, the anterior horns of the lateral ventricle were present bilaterally. At the level of the optic chiasm (2nd cut), from which the interhemispheric fissure was absent, septum pellucidum was not seen and small monoventricle was recognized. Behind this(3rd cut), inferior horns appeared bilaterally and the body portions were pin-head sized and fairly separated, not by the septum pellucidum, but by a part of cerebrum (Fig. 6E). At the level of the splenium of the corpus callosum (6th cut), monoventricle was seen again and even larger than the former. Behind the splenium (8th cut), the interhemispheric fissure was present again and rudimentary posterior horn was seen in the right side. Corpus callosum was present, but indistinct due to the fusion of the interhemispheric fissure. The corpora striata were seen in the normal site. Two thalami were separated by the 3rd ventricle. Hippocampus had relatively normal gyral pattern bilaterally. Sections from the medial side of the temporal lobe, where small blood vessels were abnormally proliferated, showed polymicrogyria. In case I, the interhemispheric fissure was completely present. It appeared to be widened and covered with a thin membrane which was turbid and yellowish (Fig. 1C). This membrane attached to the upper portion of the interhemispheric surface and extended ventrally to the orbital and hypothalamic area.

Characteristically the left lobe showed a large defect (3.1×1cm) with broad communication between the ventricle and the surface of the brain at the parasaggital portion of the frontal lobe (Fig. 1C). Sections from the cortex bordering the defect showed micropolygyria. Two cerebral hemispheres had different and abnormal gyral pattern. Medial aspect disclosed that many structures such as cingulate gyrus, corpus call-

Table 2. Changes of the prosencephalon in holoprosencephaly

Case No.	Interhemispheric fissure	Olfactory tract	Corpus callosum	Corpora striata	Thalami
I	present	absent	absent	separated	separated
II	absent	absent	absent	fused	fused
III	absent	absent	absent	fused	fused
IV	absent	absent	absent	fused	fused
V	posterior 1/2	absent	absent	fused	fused
VI	absent	absent	absent	fused	fused
VII	posterior 1/2	absent	present	fused	fused
VIII	absent	absent	absent	fused	fused
IX	absent	absent	absent	separated	fused
X	absent	absent	absent	fused	fused
IX	middle 1/2	present	present	separated	separated

Table 3. Endocrine dysgenesia and Changes of the Pyramidal tract & Cerebellum

Case No.	Pituitary ant.; post.	Adrenal gland	Thyroid gland	C.P. and Pyramid	Cerebellum
I	amorphous mass	—	—	N	—
II	—	—	—	absent	—
III	—	N(6.8)*	N(1.1)	absent	D?
IV	N; hamartoma	N(4.8)	N(1.2)	absent	
V	amorphous mass	hy.(—)	hy.(—)	absent	D
VI	amorphous mass	hy.(0.5)	hy.(—)	absent	N
VII	amorphous mass	N(7.7)	hy.(—)	absent	N
VIII	N; absent	N(9.9)	N(—)	absent	D,H
IX	N; absent	hy.(1.1)	N(—)	hy.	D,H,hern.
X	—	—	—	absent	—
XI	N; absent	—	—	absent	N?

N; Normal D; Dysplasia CP; Cerebellar peduncle
hy.; hypoplasia H; Heterotopia —; Not examined
* A parenthesized number indicates the weight of each organ in grams.

osum, fornix and septum pellucidum, were not present. The head of the caudate nucleus and anterior cerebral artery were present in the right lobe, but could not be identified in the left lobe (Fig. 1D,E). The left thalamus appeared to be relatively small and bulging out medially. No massa intermedia was present.

At the region of the pituitary stalk, examined 8 cases showed variable malformations. Four cases were represented by the amorphous masses. Sections from these, except case I which was not examined microscoprcally, revealed irregular proliferation of neuroglial cells and many capillaries with or without neuronal cells. Case VIII had unusually long adenohypophysis, but neurohypophisis was absent. In case IV, small adenohypophysis was seen. But at the area of neurohypophysis. a large hamartomatous mass was present. This mass consisted of 2 cell types. One was glial cell and the other cell was very similar to the cell present in the pallium. The latter was present in the form of rosettes or nests which were morphologically similar to neuroepithelioma.

And sheets of this cell formed a part of lining of the cystic cavity. Examination of the sella turcica in case IX revealed that this region was connected to the persistent Rathke's pouch remnant which was a thick-walled diverticular structure protruding into the nasopharynx. And sections from the sella turcica showed small adenohypophysis and a thick layer of the connective tissue. Neurohypophysis was absent. Characteristically, tissue of adenohypophysis was also found in the wall of the Rathke's pouch remnant.

Sections from the hypophysial stalk showed glial cells only without neural bundles. The optic recess of the 3rd ventricle was represented by the multiple ependymal tubules. Case XI had normal adenohypophysis but neurohypophysis was absent.

While cases III, IV and VIII among which case IV and VIII had adenohypophysis and case III was not examined, have normal adrenal and thyroid glands. Case V, VI and VII, in which pituitary gland was represented by the amorphose mass, had small thyroid glands that consisted of the nests of follicular cells and small follicles without colloid. Adrenal cortex was thin without fetal zone in case VI. But case VII had normal adrenal gland. In

case IX, although tissue of adenohypophysis was present, adrenal gland was very small and atrophic. Thyroid gland appeared to be relatively normal but it was small in size and diameter of the follicle was more variable than other normal thyroid.

Cerebral peduncles and pyramids were examined in all cases. They were present in case I but asymmetric in size. In case IX, they were hypoplastic. In other cases, they were totally absent or rudimentarily present on the microscopic examination. Cerebellums were examined grossly and microscopically in 7 cases. 3 cases were normal. Focal dysplasia was found in 4 cases. In case IX, no vermis structure was seen and two cerebellar hemispheres appeared to be fused in their upper portion (Frg. 3). And tonsillar herniation around the medulla oblongata was also noted. In case VIII, two relatively normal hemispheres were asymmetrics in their orientation due to the dysplasia of the vermis. Other cases of dysplasia were identified on the microscopic esamination.

Heterotopic gray matter was found in 2 cases. In case VIII, there are compact islands of Purkinje cells mixed with granule cells underneath the dysplastic folia. In case IX, there were groups of undifferentiated cells, resembling the cells of the external granular layer on the surface of the cerebellum, in the white matter underneath the dysplasic folia and around the between the emboliform nucleus. And mixed cellnest, consisted of this undifferentiated cells and Purkinje cells, was found between the dentate nucleus and the dysplastic folia.

DISCUSSION

In our literature review, 32 cases out of 45 cases of holotelencephaly occurred in female. Sedanoet al (1963) reported that sixty percent of the cyclopia was female. It is considered that the holoprosencephaly had definite female preponderance.

About the relationship between the facial and cerebral malformation, many observations have been reported. DeMyer et al., (1963) exclaimed that the diagnosis of alobar holoprosencephaly can be made by the examination of the face, such as cyclopia and cebocephaly. And it was reported that cyclopia always has alobar type and cebocephaly usually has it (DeMyer et al., 1964).

Our cases II, III, IV and VI correspond with their descriptions. But we cannot decide whether case I would be classified as lobar type or not. It is clear that this case is not a alobar type. Therefore, we conclude that cyclopia is not always related to alobar holoprosencephaly. And in case V, cebocephaly has semiobar type. Relationship in case VII is consistent with DeMyer's report (1964).

Hypertelorism may be seen in the semilobar type and hypotelorism is a constant finding in the alobar type. But in case IX, severe hypertelorism was related to the alobar holoprosencephaly (DeMyer et al., 1963). Facionasal malformations are invariabley present in the alobar holoprosencephaly. But in our case X, normal face without hypotelorism was related to the alobar type. All things taken together, the median facio-cerebral anomalies does not always appear in various lowfully related gradations and combinations. Case X is a very atypical holoprosencephaly in several aspects. First, there was unusual interhemispheric fusion against the typical anterior-posterior gradient. It is described that failure of cleavage into the hemispheres in anterior portion was the cardinal event in this malformation. But in this case, frontal lobes were normally separated without hypoplasia. We consider this case as an exception to that description. Consequently, this case cannot be classified as any particular type. Because semilobar holoprosencephaly indicates the brain

whose interhemispheric fissure is never complete but may be indicated posteriorly, and in the lobar type, a distinct interhemispheric fissure is present, but may be interrupted anteriorly ifthe frontal neocortex is in continuity across the midline (DeMyer et al., 1963).

Unusual gradient was also present in the ventricular system from the embryological point of view, we cannot explain the fact that the body portions of the lateral ventricle are separated where the interhemispheric fissure is absent. Secondly, olfactory tracts were identified. Thirdly, corpus callosum, although indistinct, was seen. Brain malformation in case I is classified as porencephaly, but we cannot decide whether it belongs to holoprosencephaly or not. The cerebrum which was associated with aplasia of olfactory bubs and tracts and aplasia of corpus calloslum, as case I, can be classified as lobar type. But this structures may be absent in association with the porencephaly. The location of cerebral defect and associated cortical malformations can be characterizedby listing the respective arteries which supply blood to the region affected (Dekaban, 1965).

On the basis of this hypothesis, absence of the anterior cerebral artery in the left lobe is responsible for absence of the several structures, such as corpus callosum, septum pellucidum, fornix, optic chiasm and part of caudate nucleus. And it is also suggested that absence of olfactory bulb and tract, bulging out of the thalamus and widening of the interhemispheric fissure are due to the atrophy of the medical part of the frontal and parietal lobes which is supplied by the anterior cerebral artery. But absence of the olfactory tract and bulb in the right lobe cannot be explained on the basis of that hypothesis because anterior cerebral artery is present in the right lobe.

Thin membrane covering the interhemispheric fissure and defect was described by Dekaban(1965) and we suggest that this membrane act as a barrier of CSF leakage to subdural space which is possible because of the absence of septum pellucidum and roof of the third ventricle and the presence of defect.

Ventricular system in case IX was atypical in different meaning from case VI. In alobar holoprosencephaly, the roof of the cerebral ventricles is a thin membrane which may balloon out dorsally to form a cyst(DeMyer et al, 1963). And according to the shape and opening of the monoventricle, alobar holoprosencephaly is classified into the three types; pancake type, cup type and ball type (Nishimura et al, 1976). But in this case, neither the dorsal cyst nor the opening of the monoventricle was identified. And a pit of the third ventricle was opened to the subdural space.

In our cases, adenohypophysis was present in 4 out of 8 cases. Haworth et al. (1961) described absence of the pituitary gland and hypoplasia of the adrenal cortex in 2 out of 3 cases, and in addition one showed hypoplasia of the thyroid gland. It is very interesting that neurohypophysis fails to be normally developed and appears to be hamartomatous mass in 5 cases and absent in 3 out of 8 cases examined. Several reports comment on the neurohypophysis in the holoprosencephaly, but they represent alack of consensus.

Gorlin et al. (1981) reported that the pituitary gland was small, only the pars nervosa being present. Hintz et al. (1960) described that no pituitary was found in the sella turcica, and instead at the base of the brain there was a structure thought to be neurohypophysis without adenohypophysis or infundibulum. Edmonds (1950) described presence of the pituitary gland in out of 5 cases and demonstrated that it was comprised entirely of anterior lobe without neural components. Furthermore, Yakovlev (1959) observed that profound disorganization

of mesodermal and ectodermal tissue derivatives at the septohypothalamic and infundibular region of the midline of the forebrain. On the basis of our observation, we consider that abnormal growth or aplasia of the neurohypophysis is one of the most important changes in the holoprosencephaly.

Heterotopias of the cerebellar gray matter are nonspecific and are not consistently associated with any particupar type of cerebellar dysplasia. Their occurrence in various types of cerebellar dysplasias have been overemphasized as evidence of a generalized disturbance of cerebellar development. From this point of view, it is noteworthy that both cerebellar dysplasia and heterotopia were identified in 2 and only dysplasia was seen in 2 out of 7 cases that were examined microscopically. Aplasia of the corticospinal tract appears to be consistent feature in holoprosencephaly (Friede, 1975).

COMMENT ON THE PATHOGENESIS

Defective embryogenesis of prechordal mesoderm has been postulated as one of the primary pathogenetic mechanism in holoprosencephaly, and many structural abnormalities have been explained on this basis. (Yakovlev, 1956; DeMyer et al., 1964; Cohen et al., 1971; Siebert et al., 1981).

But in the course of this study, we have observed a few unusual findings against this hypothesis. First, according to the Pollitzer, quoted by Yakovlev(1959), the formal origin of arhinencephaly is due to the failure of invagination of the foregut resulting in deficiency of the induction material in the rostral median zone of the prosencephalic plate. And Yakovlev (1959) explained the disorganization of mesodermal and ectodermal tissue derivatives at the infundibular area was due to this deficiency of the induction material. But in our case XI, evagination of the olfactory buds and anterior cleavage of the prosencephalon were recognized, while the disorganization was unchanged. This phenomenon was also seen in case I except absence of the olfactory tracts. And that report (Yakovlev, 1959) continued to describe that there was a distinct gradient of the disorder of tectogenesis from this pivotal zone of the forebrain where the nervous system is intimately bound to foregut, to the nearly normal differentiation of the cerebral plate dorsally and caudally. But in case XI, unusual interhemispheric fusion and ventricular system against this anterior-posterior gradient was seen.

Second, the association of median facial anomalies with holoprosencephaly have been explained by the induction of the rostral neural ectoderm and median facial bones by prechordal mesoderm. But in our cases, the severity of the facial malformation did not necessarily correlate with that of cerebral malformation. Especially, among these cases, cyclopia showed definitive cleavage of the prosencephalon in case I, and normal face was associated with the alobar holoprosencephaly in case X.

Third, Yakovlev described that the hindbrain and spinal cord, induced by the mesoderm of the notochord, developed normally in most instances in spite of the malformation of the prosencephalon which is induced by the prechordal mesoderm. In our series, both cerebellar dysplasia and heterotopia were identified in 2 cases and only dysplasia was seen in 2 out of 7 cases. The developmental anomalies of the cerebellum were often associated with the chromosomal abnormalities, especially trisomy 13 syndrome (Terplan es al., 1966). But in case VII, which was the only case of chromosomal anomaly (trisomy 13 syndrome) neither cerebellar dysplasia nor heterotopia was identified. Therefore cerebellar anomalies in our series are not neces-

rily caused by the chromosomal abnormalities.

SUMMARY

A total of 11 cases of holoprosencephaly was presented and analyzed. There was an obvious female preponderance. The severity of the facial malformation did not always correlate with that of the cerebral malformation. Especially, cyclopia was not associated with the alobar holoprosencephaly in 1 case. And normal face was related to the alobar type in another case. In the third case, unusual interhemispheric fusion and ventricular system against the typical anteriorposterior gradient was seen. In the other case, the single cavity was separated from the 3rd ventricle.

Neurohypophysis failed to be normally developed and appeared to be hamartomatous mass in 5 cases and was absent in 3 out of 8 cases. Cerebellar dysplasia and heterotopia were identified in 2 cases, and focal dysplasia was present in 2 out of 7 cases.

And we found that a few facts observed in our series are not explained by the pathogenetic hypothesis which has ever been presented.

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=국문초록=

전종뇌의 신경해부학적 검색

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전종뇌는 중추신경계 발달단계의 제 2 기인 전뇌가 대칭성 좌우 반구로의 분화과정에서 발생하는 심각한 기형으로서 많은 경우 얼굴중앙부를 침범하는 각종 기형을 동반하게 된다. 이러한 전종뇌의 발생기전에 있어서 발생기의 뇌주위에 위치하고 중배엽성 조직의 유발효과가 대단히 강조되어 왔으며 또 증례에 따라 전종뇌의 기형 정도도 상당한 차이를 나타내어 학자들간에 그 발생기전에 대한 많은 관심이 경주되어 왔다.

저자들은 1976년 이래로 서울대학교 의과대학 병리학교실에서 검색된 것과 외부에서 의뢰된 예들을 합하여 총 11예의 전종뇌증례를 분석하여 안면 및 기타부의 기형과 중추신경계의 기형과의 관계를 추궁하였고 특히 전종뇌의 해부학적 특징을 기술하였다.

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LEGENDS FOR FIGURES

Fig. 1. Case Ⅰ.

A: Face showed, from the bottom, synotia, cyclopia, proboscis and malformed oral cavity (protruded mass).

B: Ventral view. Thin optic nerves and disorganization at the infundibular area are seen.

C: Anterior view. The interhemispheric fissure is completely present beneath the covering membrane. And a large cerebral defect was seen in the left lobe.

D: Medial view of the right lobe.

E: Schematic view of microscopic structure of the protruded mass seen in Fig 1A.

Fig. 2. Case Ⅴ.

A: Cebocephaly was related to the semilobar holoprosencephaly. Left eye showed conjunctival coloboma

B: Serial coronal sections of the brain.

Fig. 3. Case Ⅸ.

A: Face with hypertelorism and arhinia was related to the alobar holoprosencephaly.

B: Posterior view of the brain showing characteristic alobar holotelencephaly.

Fig. 4. Case Ⅹ.

Relatively normal appearing face was related to the alobar holoprosencephaly.

Case Ⅲ.

A: A single eyeball shows coloboma of iris.

B: A huge proboscis like mass was protruded from all the region of the forehead.

C: Dorsal view of the brain showing completely exposed 3rd ventricle.

D: Coronal sections of the brain disclosed obliteration of the single cavity which does not connect with the single cavity which does not connect with the 3rd ventricle nor have the opening.

E: A pit of 3rd ventricle was opened to the subdural space.

Fig. 5. Case Ⅸ.

A: Normal face.

B: Middle hafl shows the fusion of the two hemispheres. Dorsal view.

C: Ventral veiw. Olfactory tracts are present in the olfactory sulcus. And disorganization at the infundibular area was seen.

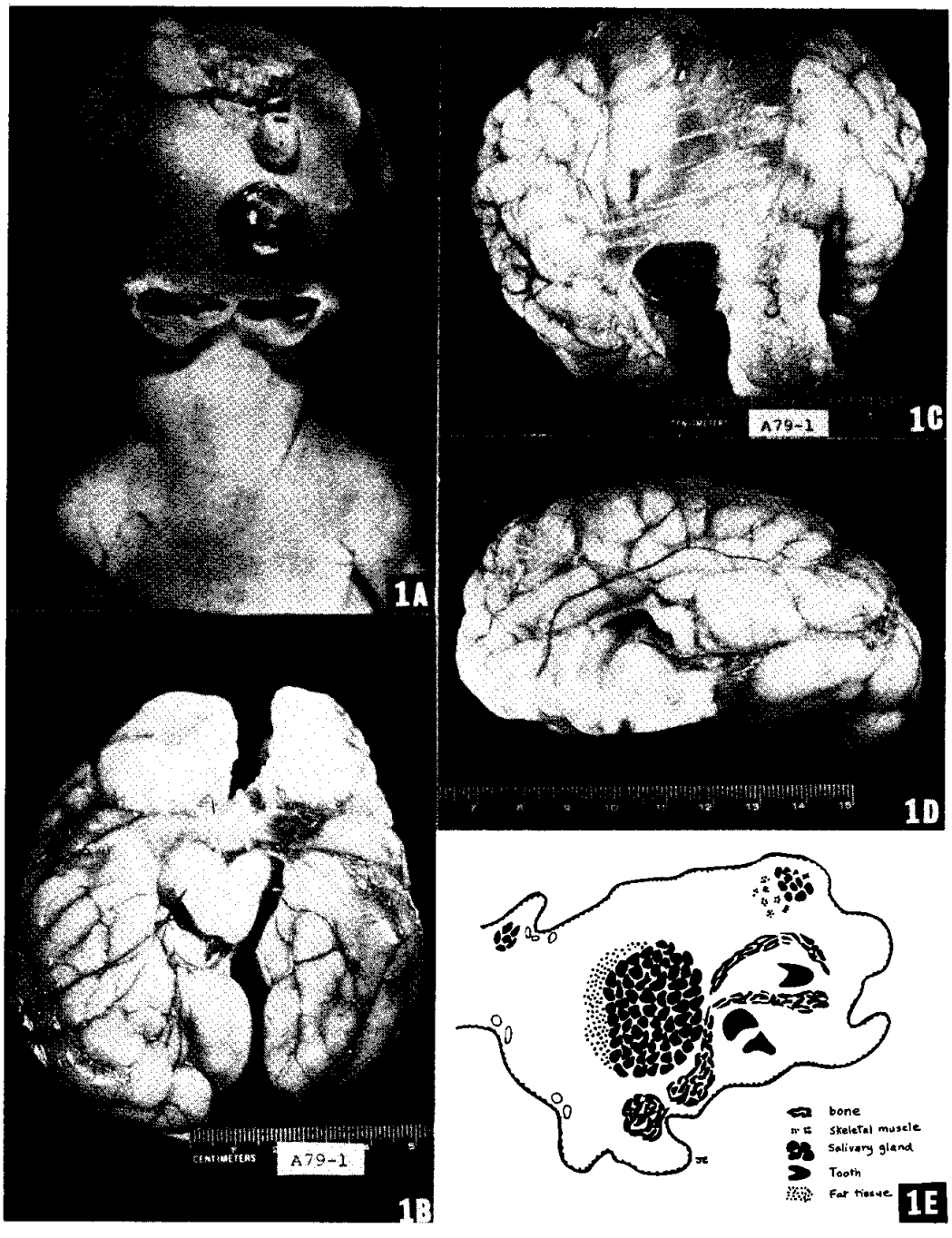
D: Coronal sections of the cerebrum showed unusual changes of the ventricular system.

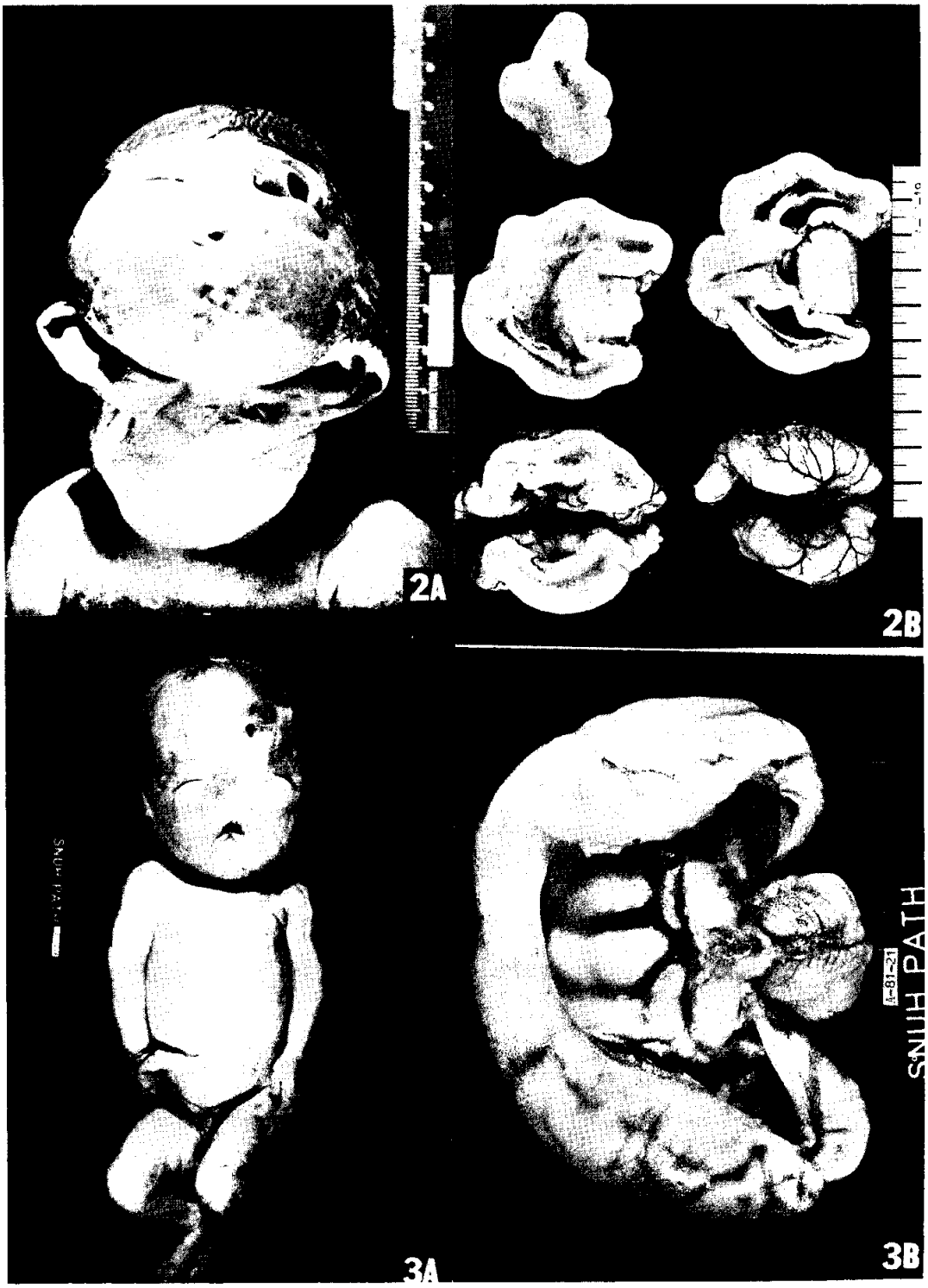
E: 3rd cut. Teh body portions of the lateral ventricle are pinhead sized and fairly separated by a part of cerebrum.

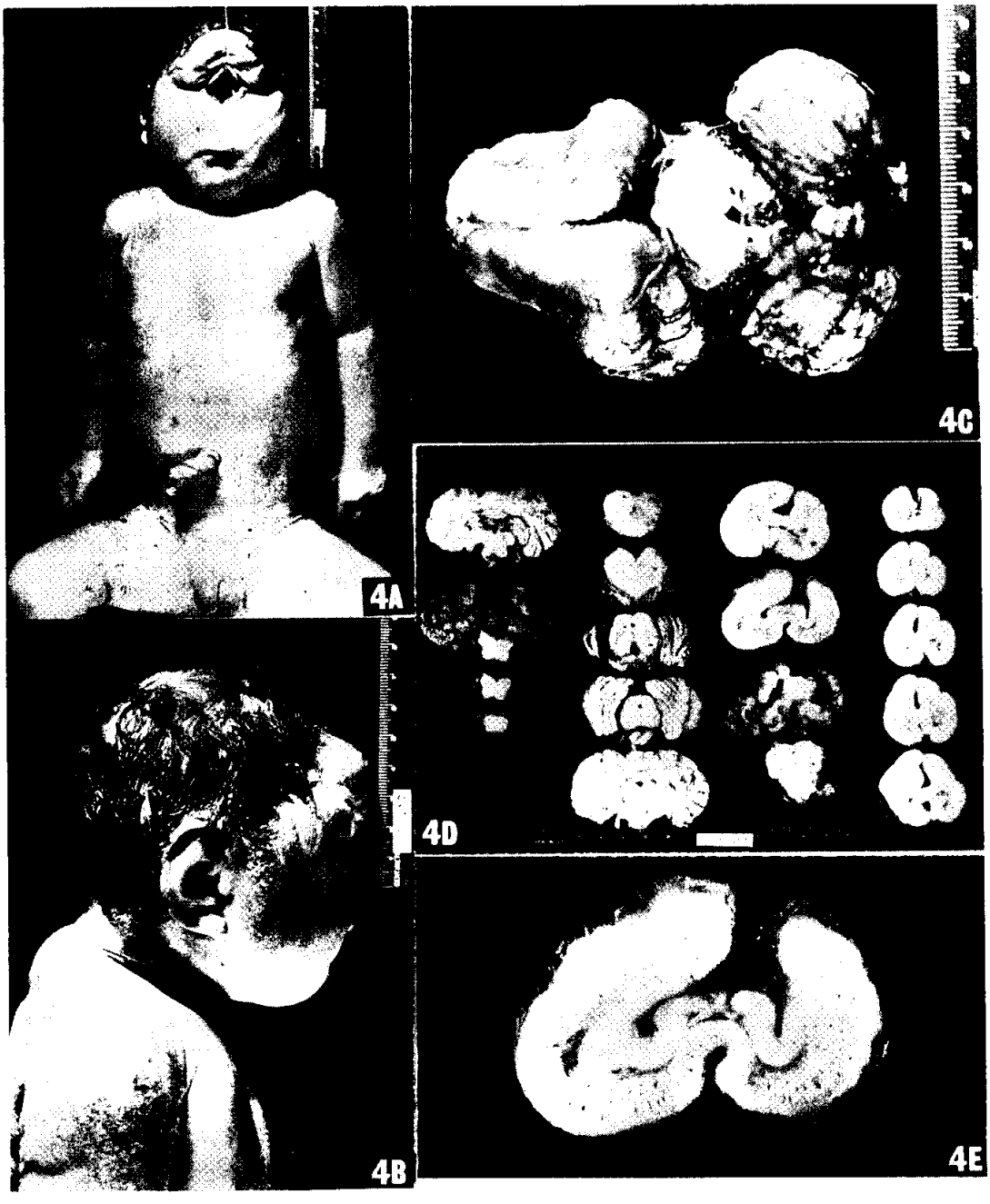
F: Schematic reconstruction of the ventricular system. Left: dorsal view right: medial view of the right lobe Number represents the sequence of the cutting. Dotted line outlines imaginary shape and arrow indicates the posterior horn of the lateral ventricle. Note that the two lateral ventricles are separated at the 1st & 4th cuts and connected at the 2nd & 6th cuts. 3r:3rd ventricle Inf; Inferior horn of the lateral ventricle.

Fig. 6. A: Case Ⅵ. Section from the amorphous mass at the region of the pituitary stalk.

B: Case Ⅳ. Section from the large hamartomatous at the area of meurohypophysis. In this case, small adenohypophysis was present.


1A
A79-1
1C
1D
CENTIMETERS
A79-1
1B
bone
Skeletal muscle
Salivary gland
Tooth
Fat tissue
1E


2A
2B
3A
3B
SNUH PATH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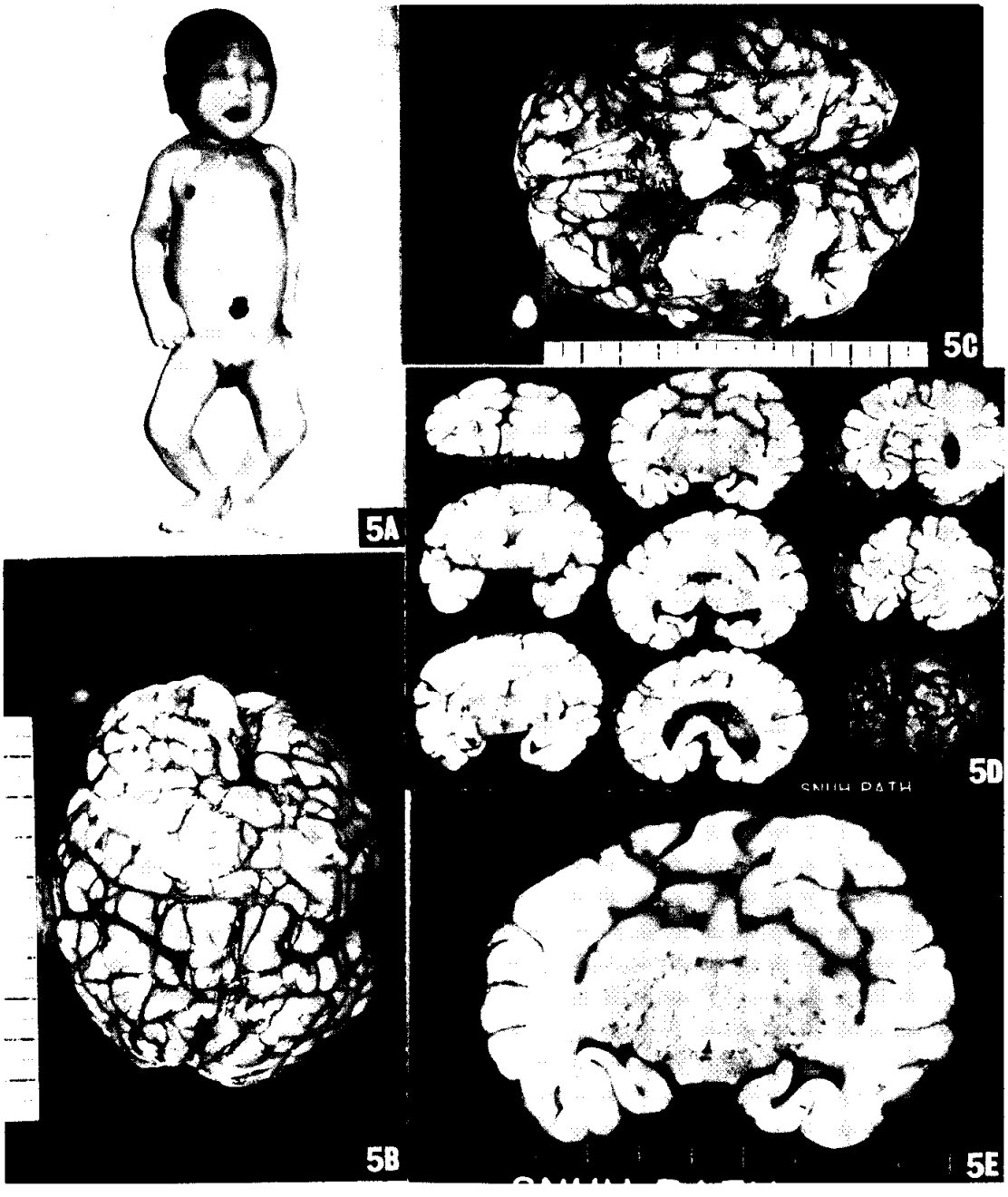
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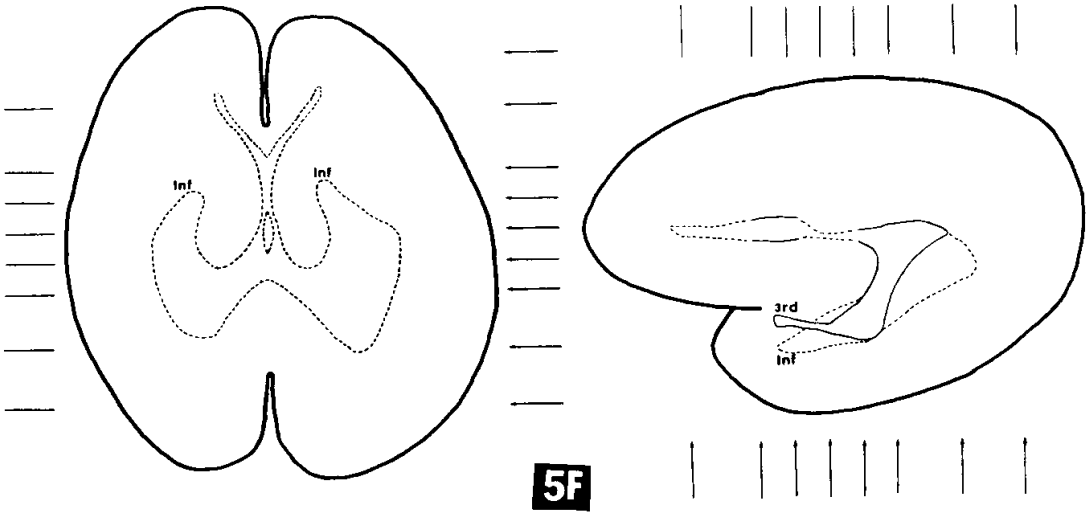
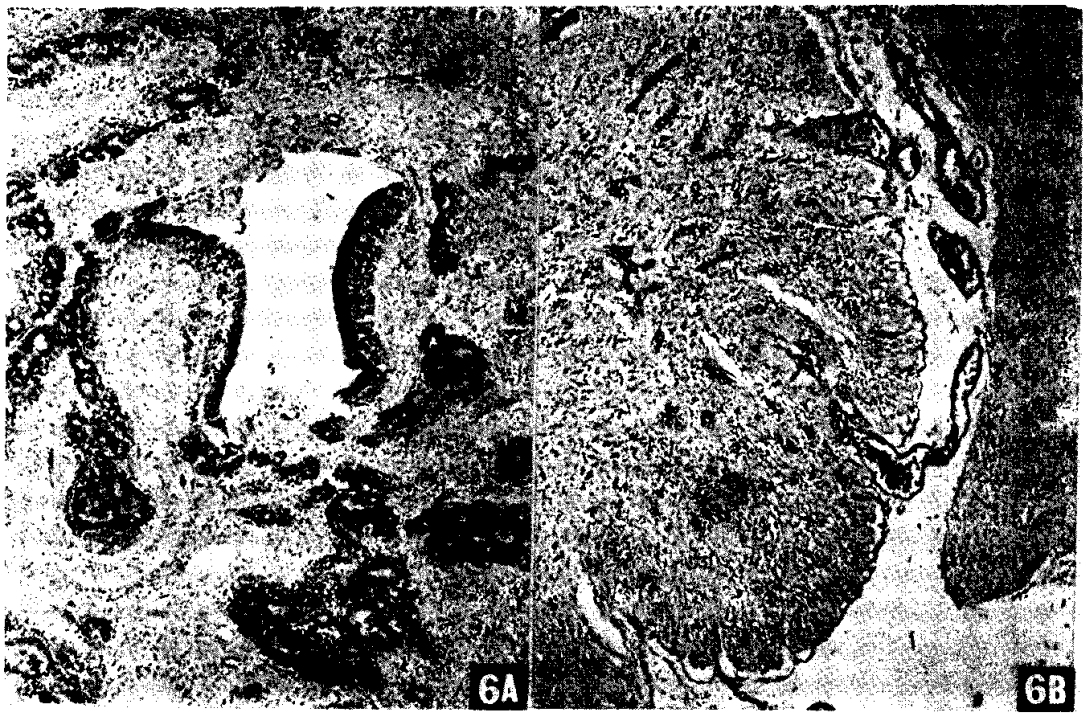


5F



6A 6B