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Pulmonary Agenesis/Hypoplasia associated with Renal Dysplasia and Persistent Cloaca. Is It on a Spectrum of the so-called Potter's Syndrome?

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= Abstract =A case of pulmonary agenesis/hypoplasia associated with intracardiac anomaly, hydrocephalus, bilateral renal dysplasia and persistent cloaca is reported. The pathogenic theories are briefly reviewed and it is suggested that the cause of this anomaly might be a primary mesodermal defect and this case might be on a spectrum of the so-called Potter's syndrome.

Key Words; ***Lung agenesis, Kidney dysplasia, Cloaca, Potter syndrome***

Agenesis of the lung is not an uncommon anomaly, and when it is an isolated finding, it is compatible with even normal life (Hochberg & Naclerio 1955; Netterville 1957; Van Loon & Diamond 1962; Shenoy 1979). Hundreds of cases were reported in the world literature (Oyama et al. 1953; Valle 1955; Booth & Berry 1967; Maltz & Nadas 1968; Borja et al. 1970). Various associated malformations are common. Recently we experienced a case of unilateral pulmonary agenesis and contralateral hypoplasia associated with bilateral renal dysplasia, cloacal anomaly, intracardiac anomaly, and hydrocephalus. The exact cause of this anomaly is unknown, but the association of other major malformations lead us to speculate the pathogenic mechanism.

CASE REPORT

This female baby was born to a 23-year-old Korean woman, para 0-0-0-0 at 33 weeks of gestation. During pregnancy she drank several times and smoked everyday, but no history of medication and viral illness was obtained. Labor began spontaneously but was complicated by cephalopelvic disproportion due to marked hydrocephalus. Transvaginal craniotomy was done and soon the baby was delivered. At birth there was no sign of life.

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An autopsy was performed on the following day and revealed a monstrous baby. Body measurements were as follows; body weight 1,725 gm:crown to rump length 31 cm:crown to heel length 50 cm:chest circumference 26 cm: and estimated head circumference 34 cm. The placenta was grossly normal and the cord had three vessels. The head showed a previous craniotomy scar and was somewhat shrunken but hydrocephalic feature was obvious. Both ears were low-set and malformed, and especially the left ear was severely malformed, having no pinna. Mild hypertelorism, flat nose, and slightly receded chin were noted in the face with cleft lip and palate. The abdomen was distended. Ambiguous external genitalia and an imperforate anus were observed. Extremities showed no grossly visible malformation but no transverse palmar crease was seen in the left hand. Plain roentgenogram of the whole body at autopsy revealed haziness in the right hemithorax and normal skeletal configuration except for the thinning and defect of the occipital bone which was considered as a result of hydrocephalus.

The brain showed marked hydrocephalus due to aqueductal atresia. Dilatation of the third and the lateral ventricles, thinned anterior cerebral mantle and smooth ventricular surfaces were noted. Also observed was an absence of septum pellucidum. The cerebellum was quite small. On opening the

chest wall, the right lung was absent, right hemithorax was filled with fatty tissue and shifted heart and mediastinal structures. The left lung was hypoplastic (5.6 gm) but had two lobes with normal bronchial distribution. Microscopic examination of the left lung revealed normal fetal development compatible with the 33 weeks of gestational age. The larynx and the trachea were normally developed but no remnant of the right main bronchus was seen, and the trachea smoothly switched over to the left main bronchus.

The heart revealed pentalogy, that is infundibular stenosis, atrial septal defect, ventricular septal defect, and overriding aorta. A large patent ductus arteriosus was noted. The pulmonary trunk was hypoplastic and gave no right pulmonary artery, directly extending into the left pulmonary artery. The left lung was drained to the left atrium via a single pulmonary vein. No thymic tissue was discovered in the thoracic cavity. A large cyst-like structure was seen in the lower abdomen and the intestines were pushed upward. The intestines were very short and had a Meckel's diverticulum 25 cm above the ileocecal valve. The cyst-like structure was uterus, and on opening it, whitish fluid gushed out, revealing hydrometrocolpos with stenotic cervix. Both tubes and ovaries were present, and microscopic examination showed hypocellular ovary with increased interstitial collagen tissue. The vagina was atretic and was connected to the obstructed urethra anteriorly and to the rectum posteriorly, revealing persistent cloaca. From the bladder both ureters were connected to the kidneys. The kidneys were severely dysplastic with multiple cysts of varying size, and both ureters showed hydroureter. Microscopic examination of the kidney showed hyaline cartilage islets and primitive tubules between the cysts. Relatively well preserved glomeruli and convoluted tubules were occasionally noted in groups but no collecting tubules were observed. The adrenals were large and showed prominent fetal cortex. Histologic slides of the liver showed massive extramedullary hemopoiesis in both the parenchyme and the interstitium but was considered normal for this age.

Summary of the autopsy findings

1) Hydrocephalus due to aqueductal atresia
2) Pentalogy (TOF, ASD)
3) Agenesis of the right lung and hypoplasia of the left lung
4) Agenesis of the thymus
5) Persistent cloaca
6) Bilateral dysplasia of the kidneys
7) Facial anomalies; cleft lip and palate, low set malformed ears, flat nasal bridge, receded chin
8) No transverse palmar crease, left hand

DISCUSSION

Developmental arrest of the lung has been classified by Schneider(1912) into three groups: a group in which there is complete absence of bronchi, alveolar tissue, and their blood supply (agenesis); a group in which a rudimentary bronchus arose from the trachea with to pulmonary tissue investing its tip (aplasia); and a group with poorly developed main bronchus invested by a fleshy mass of ill-developed pulmonary tissue (hypoplasia). Associated anomalies are common and include especially cardiovascular, genitourinary, and musculoskeletal anomalies. In the embryo, the lungs first appear at 3 mm stage (approximately 24 days of ovulation age) and at 26 to 28 days, right and left lung buds arise separately. At 8 mm stage (30 to 32 days) lobar bronchi appear as outgrowths of the primary bronchi (Boyden 1955). So agenesis of the lung indicates a developmental defect occurred at the very early embryonic period and hypoplasia may be a defect happened somewhat later.

The cause of pulmonary agenesis/hypoplasia is not clear but several theories are present. Mechanical interference can cause pulmonary hypoplasia as in the diaphragmatic hernia, eventration of diaphragm, extralobar pulmonary sequestration, and other intrathoracic mass lesions, but agenesis clearly due to intrathoracic space occupying lesion is not reported. Viral agent can cause abnormalities of the heart and may be a cause of lung malformation (Tuyman & Gardner 1952), but no specific pulmonary malformation caused by virus is reported. Wilson and Warkany observed that pulmonary agenesis occurred in the offspring of rats fed with vitamin A deficient diets (Wilson & Warkany 1949). Such a view cannot be accepted as a cause of human pulmonary agenesis because of such a severe malnutrition doesn't exist in the present society, especially in the developed countries.

Pulmonary hypoplasia associated with bilateral renal agenesis makes the so-called "Potter's syndrome". The classical features of the Potter's syndrome include bilateral renal agenesis, pulmonary hypoplasia, Potter's face, and skeletal abnormalities

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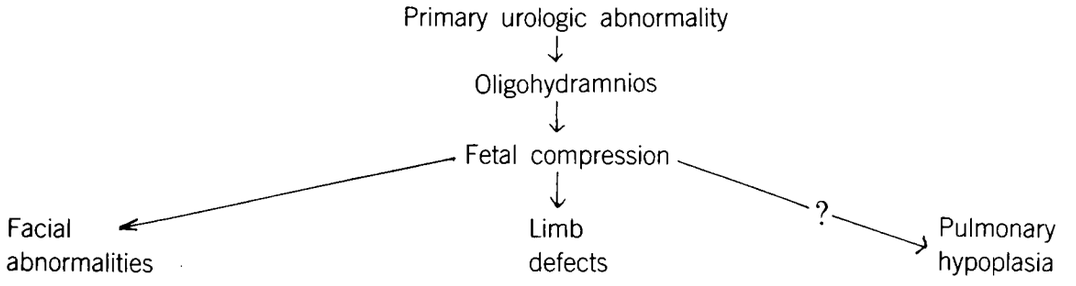

SCHEME II

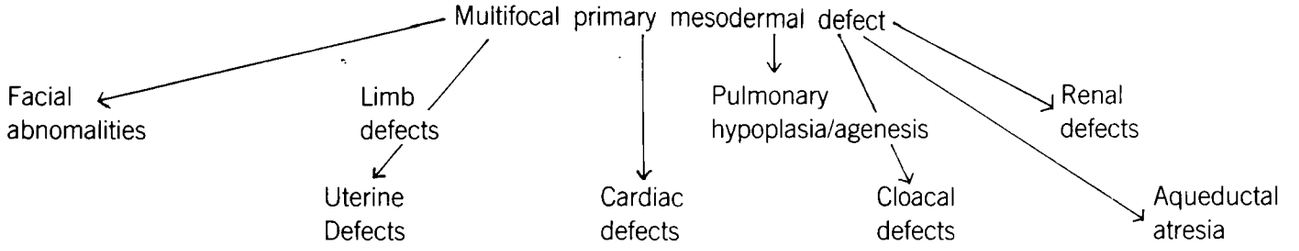

Fig. 1. Fitch and Lachance's new scheme, modified by us.

but renal dysgenesis and other features are also included in the varieties. The cause of pulmonary hypoplasia and other nonrenal features of the Potter's syndrome has been generally thought to oligohydramnios due to a lack of production of urine by anephric fetus (Perlman & Levin 1974; Thomas & Smith 1974). But oligohydramnios theory cannot explain all the features of Potter's syndrome such as prominent epicanthic fold, growth deficit, increased incidence among males, and the high frequency of other associated malformations (Potter 1974). There are rare cases in which polyhydramnios was associated with primary pulmonary hypoplasia (Mendelsohn & Hutchins 1977) or with Potter's syndrome (Pashayan et al. 1974). There is also an interesting case in which unilateral renal agenesis and contralateral renal dysplasia was associated with bilteral pulmonary agenesis, complex intracardiac anomaly, and polyhydramnios of 3000 ml (Lee et al. 1969). Recently the oligohydramnios theory was challenged, and Fitch and Lachance (Fitch & Lachance 1972), suggested a new scheme that multifocal primary mesodermal defect might be the cause of Potter's sysndrome and other anomalies involving both the kidney and limb (Fig. 1). Kallen and Winberg (1974) suggested that Potter's syndrome and sirenomelia are on the one spectrum of disease involving the caudal mesoderm, and that Potter's face and pulmonary hypoplasia may be caused by a cranial extension of such a mesodermal defect (Kallen & Winberg 1974). Page and Stocker (1982) agreed to their opinion that an intrinsic factor might be the cause in the pulmonary and renal defect.

In our case, bilateral renal dysplasia and persistent cloaca were noted. Renal dysplasia is generally believed to occur as a result of urinary obstruction in early embryonic period (Bernstein 1971), and in our case, persistent cloaca with urethral obstruction seems to be the cause. The cloaca is first seen at approximately 4 weeks of age as a part of hindgut lying caudal to the allanotic opening. Persistent cloaca results from the failure of the urorectal septum formation, which is normally completed at 17 mm stage (seventh week). The exact relationship of urorectal septum to abnormal development of the genitourinary tract is still unclear, but associated genitourinary tract malformation is found in 60 to 80 percent of the cases (Cheng & Fisher 1974).

When three or more malformations occur in an infant, it can rarely be caused by three or more unrelated teratogens (Kallen & Winberg 1968). Therefore it is conceivable to think that multiple malformations are somehow interrelated. In our case, pulmonary agenesis/hypoplasia, cardiac anomaly, hydrocephalus, renal dysplasia, and persistent cloaca might be caused by one intrinsic cause, and persistent cloaca might be caused by one intrinsic cause, and persistent cloaca might be caused by one intrinsic cause, that is faulty

mesodermal development since very early embryonic stage. Perhaps our case might be on a spectrum of the so-called Potter's syndrome due to a primary mesodermal defect. Of note is the remarks of Booth and Berry (1967), in their review of unilateral pulmonary agenesis, on the ipsilateral facial, jaw, limb, and renal abnormalities with unilateral pulmonary agenesis. Such a finding might be a result of unilateral mesodermal defect affecting only ipsilateral side of the body. Other cases showing ipsilateral abnormalities with unilateral lung agenesis were reported by several other authors (Gorlin et al. 1963, Kenawai & Dickson 1976; Mygind et al. 1980). DeBuse and Morris suggested a defect of vascular development and genetic background as a cause of this anomaly (DeBuse & Morris 1973). But such an extensive vascular maldevelopment is less likely in our case and other unknown inherent mesodermal defect is more likely.

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= 국문초록 =

Potter 증후군 변형의 1예

서울대학교 의과대학 병리학교실

지제근 · 송영기 · 손진희

저자들은 신생아의 1부검예에서 일측성 폐무형성, 선천성 심기형, 수뇌증, 양측성 신이형성증 및 총배출강 존속증이 수반된 것을 관찰하고 이것이 우연한 수반현상이라기 보다 Potter 증후군의 한 변형으로 이해하는 것이 기형발생학적으로 더욱 타당하다고 사료되어 본 증례를 보고하였다.

LEGEND FOR FIGURES

Fig. 2. Face showed hypertelorism, low set ears, receding chin, cleft lip and palate, absence of the pinna on the right ear, and flat nasal bridge.

Fig. 3. On opening the thoracic cavity, heart and mediastinal structures were displaced to the right side and no lung tissue was found in the right hemithorax.

Fig. 4. No bronchial bud to the right side was seen. The left lung was hypoplastic. The white material on the right side is the fatty tissue found in the right hemithorax.

Fig. 5. In the abdomen, hydrometrocolpos and persistent cloaca were found.

Fig. 6. Both the kidneys were severely dysplastic with multiple cysts.

Fig. 7. Coronal sections of the brain shows extreme hydrocephalus and the absence of the septum pellucidum.

Fig. 8. Microscopic view of the left lung shows normal alveolar development.

Fig. 9. Microscopic examination of the kidneys shows severe dysplasia represented by heteroplastic cartilage islets and primitive ductules.

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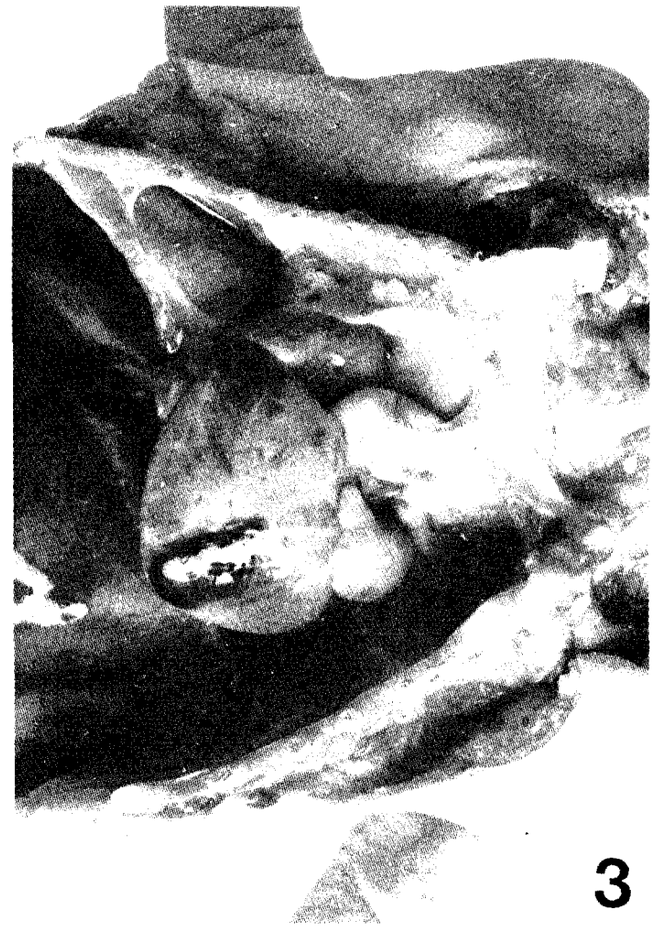

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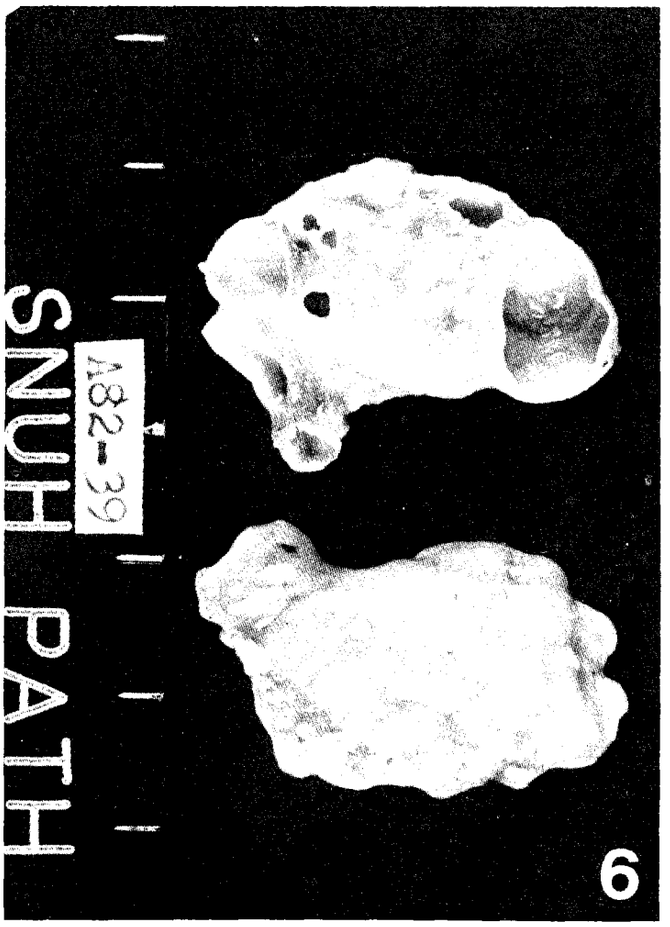
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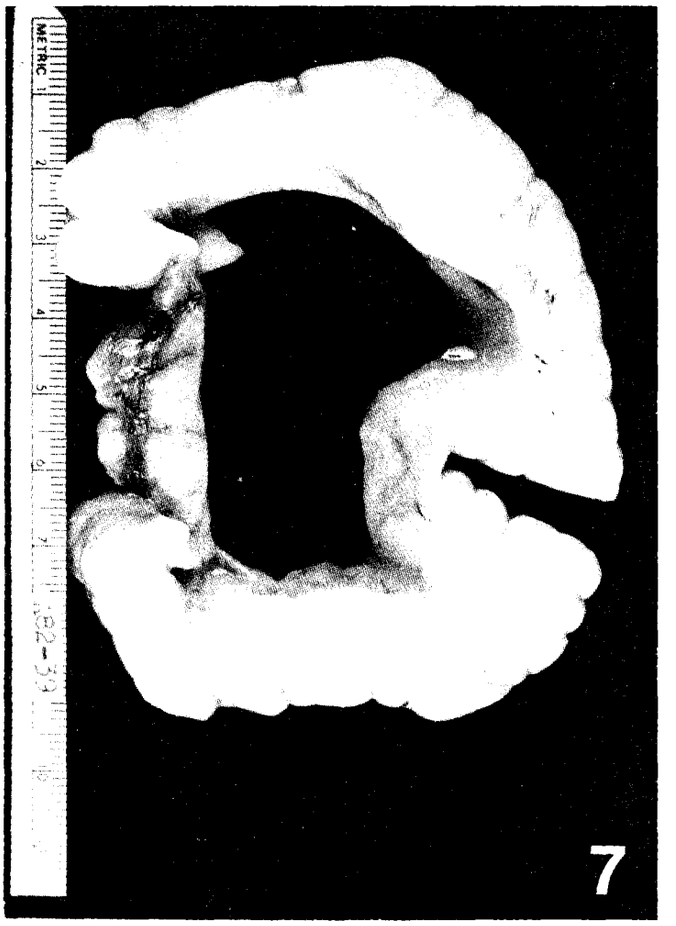
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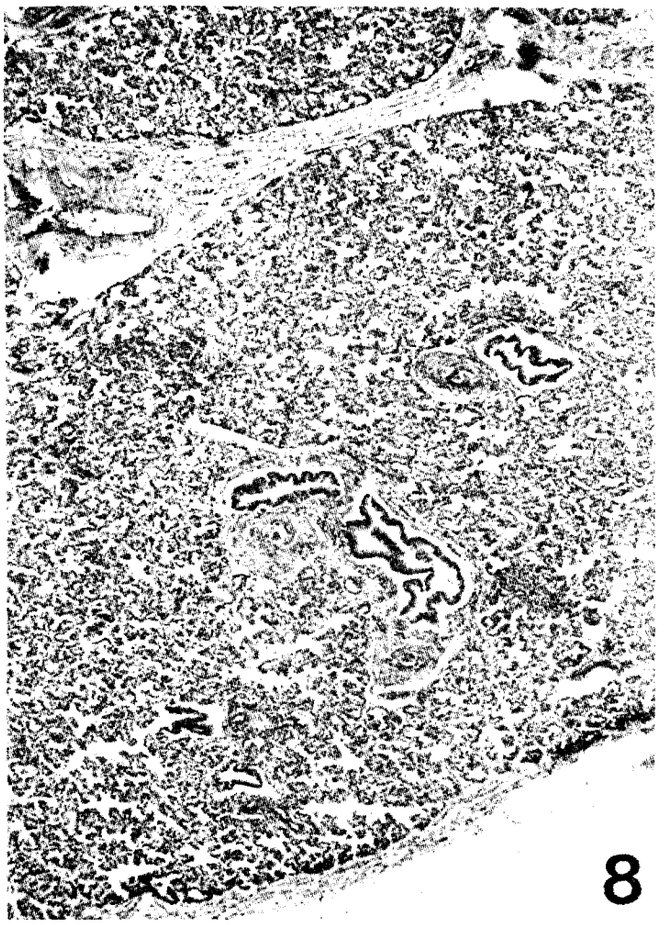
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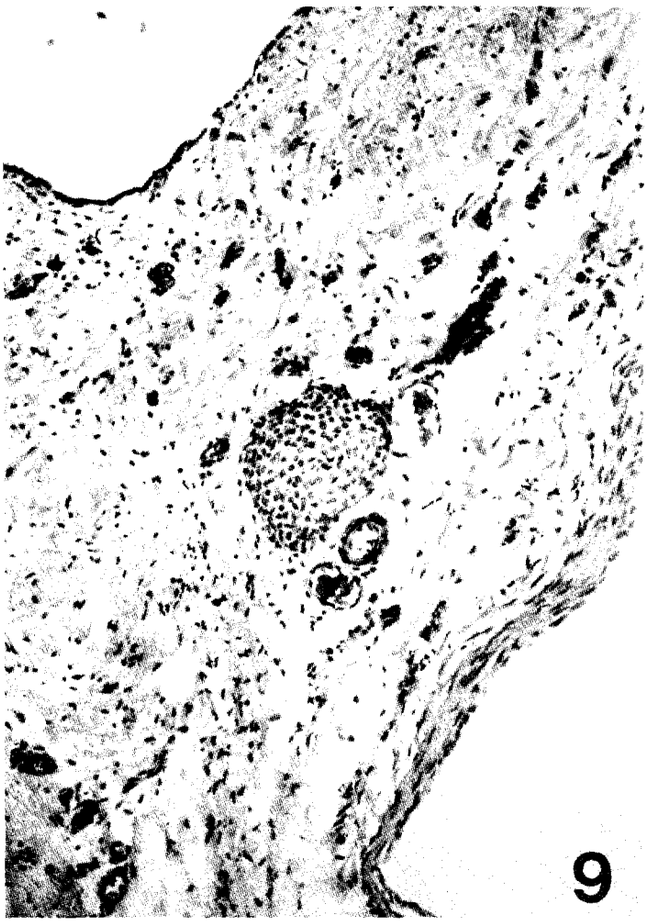
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