

Listeriosis in a Stillborn Fetus (An Autopsy Case)

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= Abstract = Listeriosis is an infectious disease of animals and man that is characterized by a wide spectrum of clinical manifestations. Miliary granulomatosis is unique features of listeria infection in deadborn fetuses and enwborn infants.

This report deals with an autopsy case of miliary granulomatosis in a deadborn fetus, which was thought to be due to listeria infection. The liver and spleen were enlarged and showed disseminated miliary speckles. Microscopically these nodules were composed of necrotizing granulomas showing central necrosis with nuclear debris and peripheral epithelioid cell collections. In the centers of the lesions there were numerous micro-organisms in clusters or isolated, that showed gram-positivity on Brown-Brenn stain and dark elongated structures on Warthin-Starry stain. These miliary granulomas were also seen in the lungs, intestinal tract, liver, adrenals, spleen and bone marrow.

Key words: *Listeriosis, Congenital infection, Perinatal death, Stillborn, Bacterial infection*

INTRODUCTION

Listeriosis is an important infectious disease in perinatal period because it may account for stillbirth, premature birth, and neonatal death.

There seems to be an increased awareness of this condition which, until recently, had been underreported or underdiagnosed (Robertson *et al.*, 1979; Editorial 1980, 1985). In Korea, although *Listeria monocytogenes* has been isolated in bacteriological material, such as blood and cerebrospinal fluid (Lee *et al.*, 1980), congenital listeriosis was never reported in Korean literature. It is important to recognize that the pregnant women may manifest no significant symptomatology and yet transmit the *Listeria* infection to the fetus through placenta.

This report deals with a case of congenital listeriosis in a fetus that was born dead at 30 weeks of gestation.

CASE REPORT

This was a deadborn female fetus to a 33 year old woman at 30 weeks of gestation. The fetus was sent to our Department for the postmortem examination. No further information of the pregnancy was available. The placenta was not included in the specimen.

Postmortem examination revealed a moderately macerated fetus with no gross anomaly. It weighted 1400 gms and measured 26.5 cm in crown-rump length and 42 cm in crown-heel length. The skin showed no rash. The liver was enlarged (89.4 gm) and so was the spleen (14.4 gm). The lungs showed a few petechiae on the pleura. The liver and spleen were studded with grayish white nodules on the surface (Fig. 1, 2). Cut sections showed similar millet-sized nodules scattered throughout. They measured 0.3-0.5 mm in diameter and bulged slightly on surface.

Microscopically there were necrotizing granulomas of varying maturity in most viscera examined. The lungs were scattered with granulo-

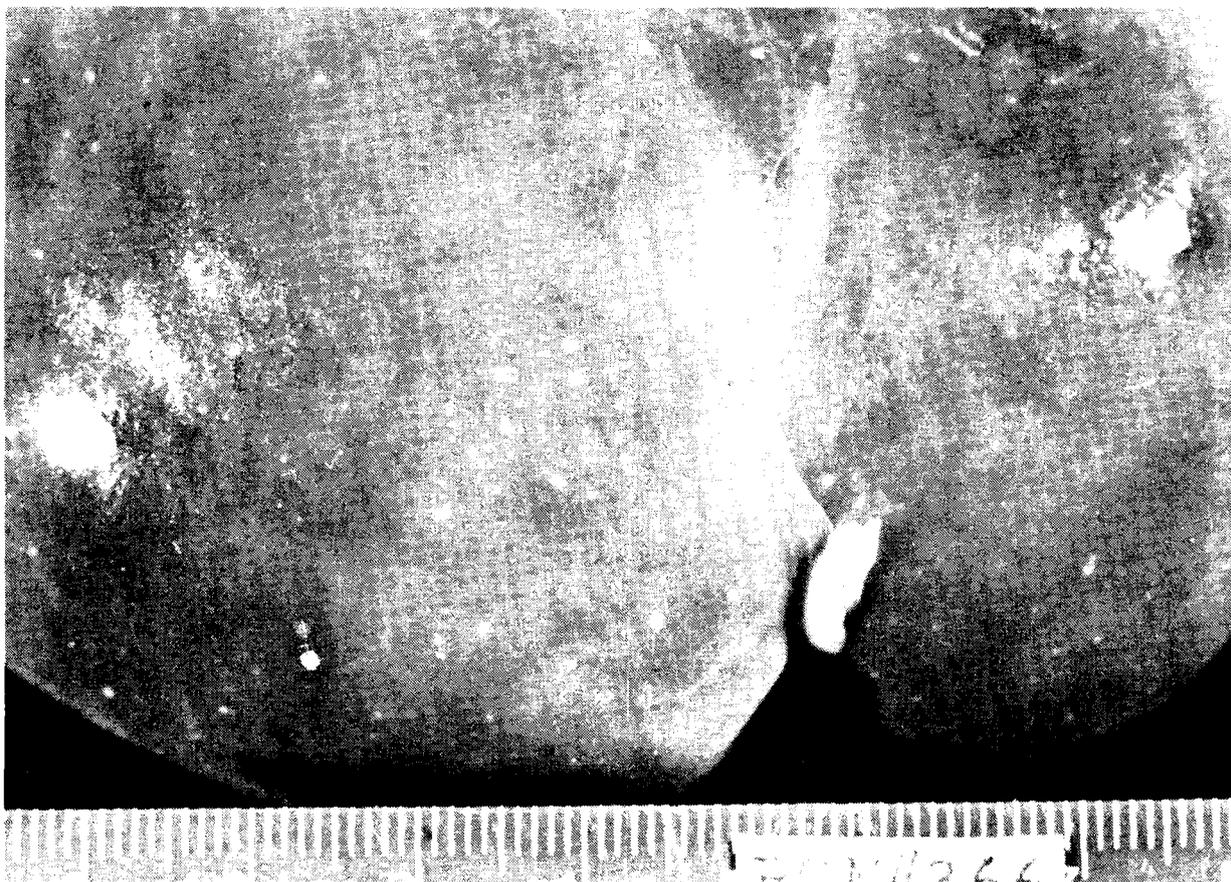


Fig. 1. Liver surface shows scattered whitish nodules in the right and left lobes. They are less than 1 mm in diameter and bulge slightly on the surface. These nodules were also seen inside the liver.



Fig. 2. Spleen shows disseminated whitish speckles on the surface.

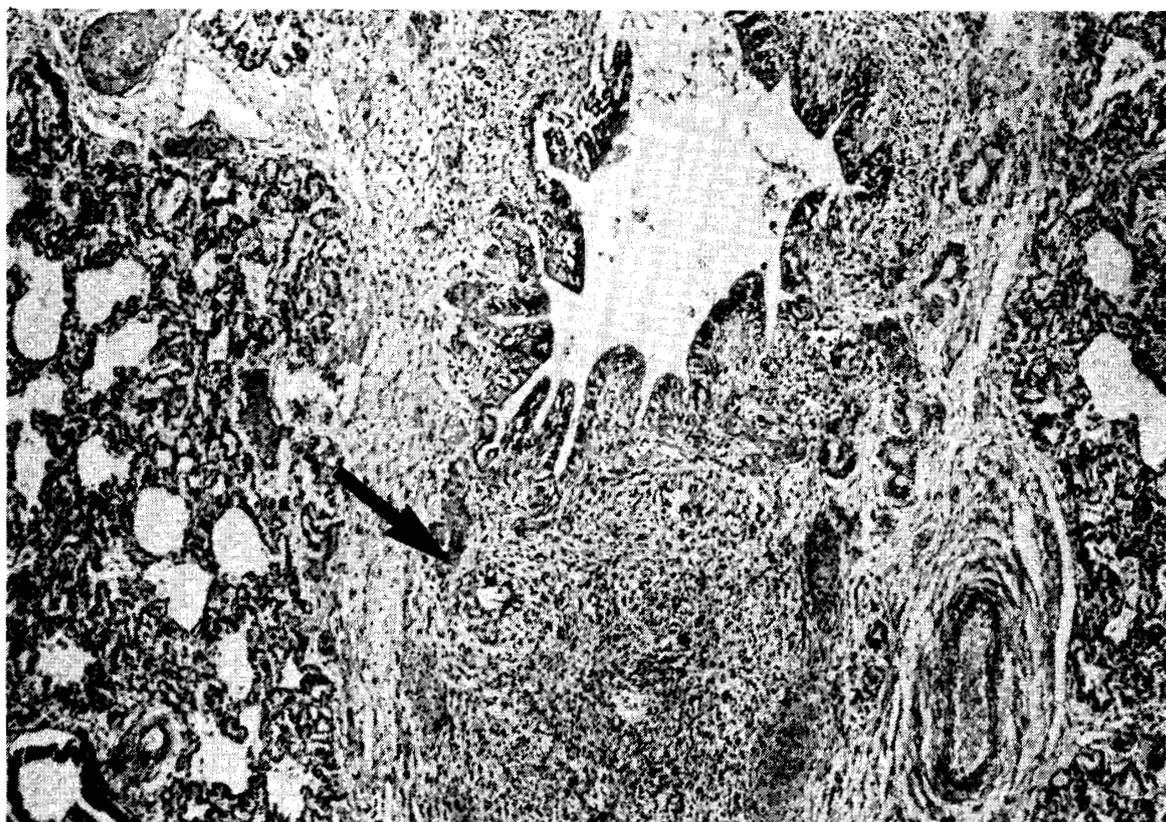


Fig. 3. Microscopic picture of the lung, showing a nodule (arrow) in peribronchial space. H & E $\times 100$.

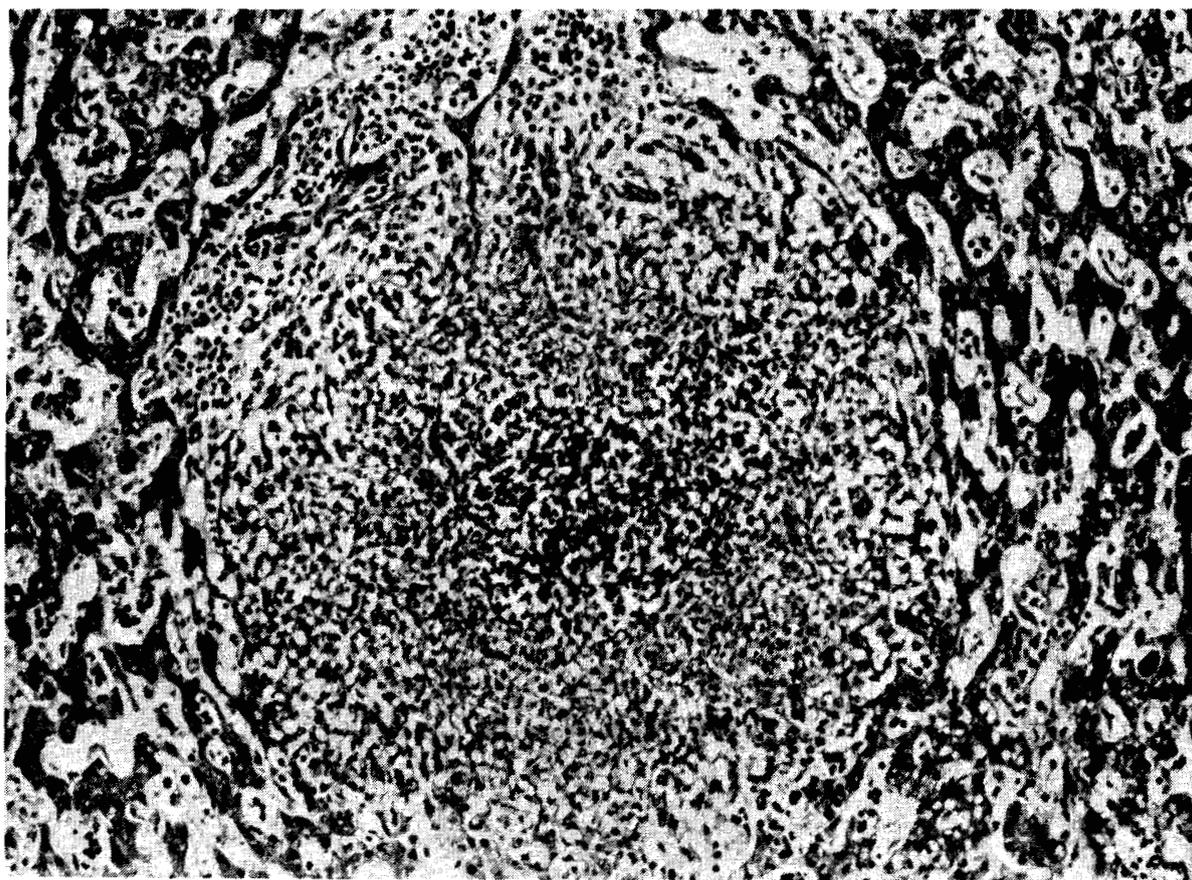


Fig. 4. Characteristic necrotizing granuloma seen in the liver, consisting of central necrosis with numerous nuclear debris and peripheral epithelioid histiocytes. Note also inflammatory cells around the granuloma. H & E $\times 250$.

mas often in and around the bronchial tree (Fig. 3). When subepithelial stroma of the bronchial mucosa was involved, erosions or ulcerations were seen. The nodules in general consisted of epithelioid histiocytes and nuclear debris with varying amount of neutrophils, lymphocytes and occasionally plasma cells. When the nodules increased in size there was often central necrosis with numerous nuclear debris and fibrin exudate, that were again surrounded by epithelioid histiocytes (Fig. 4). Langhans giant cell formation or pure epithelioid granuloma was not noted. Early lesion consisted of collections of histiocytes and some nuclear debris without acute inflammatory cells or necrotic center. In the lung a small branch of pulmonary artery (Fig. 5) was involved by necrotizing process involving entire thickness and early thrombus formation. This segmental vasculitic change was seen in several foci in the liver and other organs. The veins were more frequently involved than the arteries. The liver and adrenals were most extensive in containing necrotizing granulomas. There was a marked ex-

tramedullary hemopoiesis in the liver as well as widespread miliary granulomas (Fig. 6). In the liver the granulomas appeared to start from the lobules rather than the portal tract, and extend to hepatic cell cords associated with destruction and inflammatory change. There were a few areas where hepatic vein branches were occluded due to granulomatous endophlebitis. The adrenals showed well formed granulomas in the fetal cortex (Fig. 7). The spleen showed scattered granulomas. There was no increased phagocytic activity in the red pulps. No follicle formation was seen. Focal erosion and inflammation were noted in the esophagus and hypopharynx. There was prominent involvement of gastrointestinal tract. The lesion was located in the stomach and small intestine. In the small intestine lymphoid tissue was particularly involved by necrotizing granulomas associated with lymphoid hyperplasia (Fig. 8). A few foci of serosa also contained granulomas (Fig. 9). There were no lesion found in the heart, thyroid, thymus, ovary and urinary bladder. Central nervous

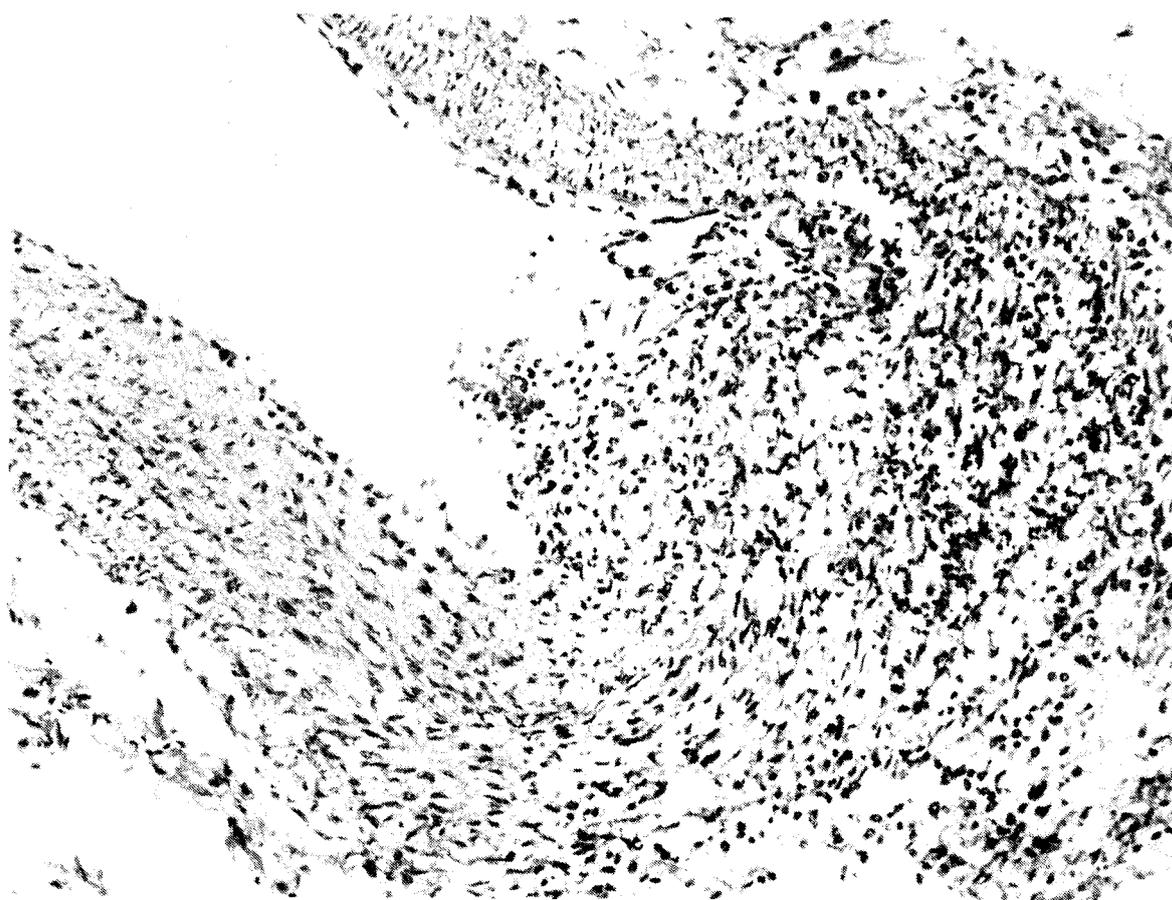


Fig. 5. Pulmonary artery branch showing a focus of transmurular vasculitic change. Here again shows both necrotic debris and epithelioid cells. H & E \times 250.

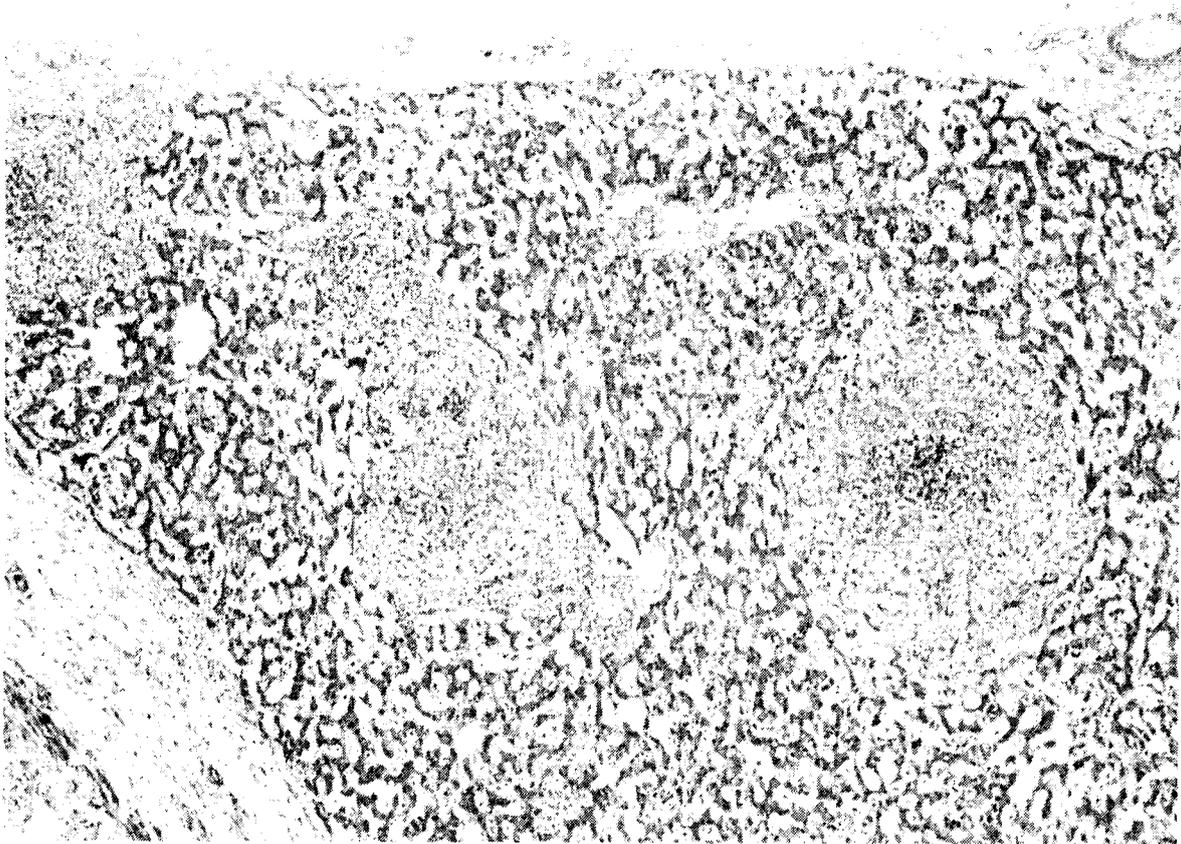


Fig. 6. Photomicrograph of the liver, showing 3 granulomas in subcapsular area. The lesions are well delineated from the surrounding normal liver. H & E \times 100.

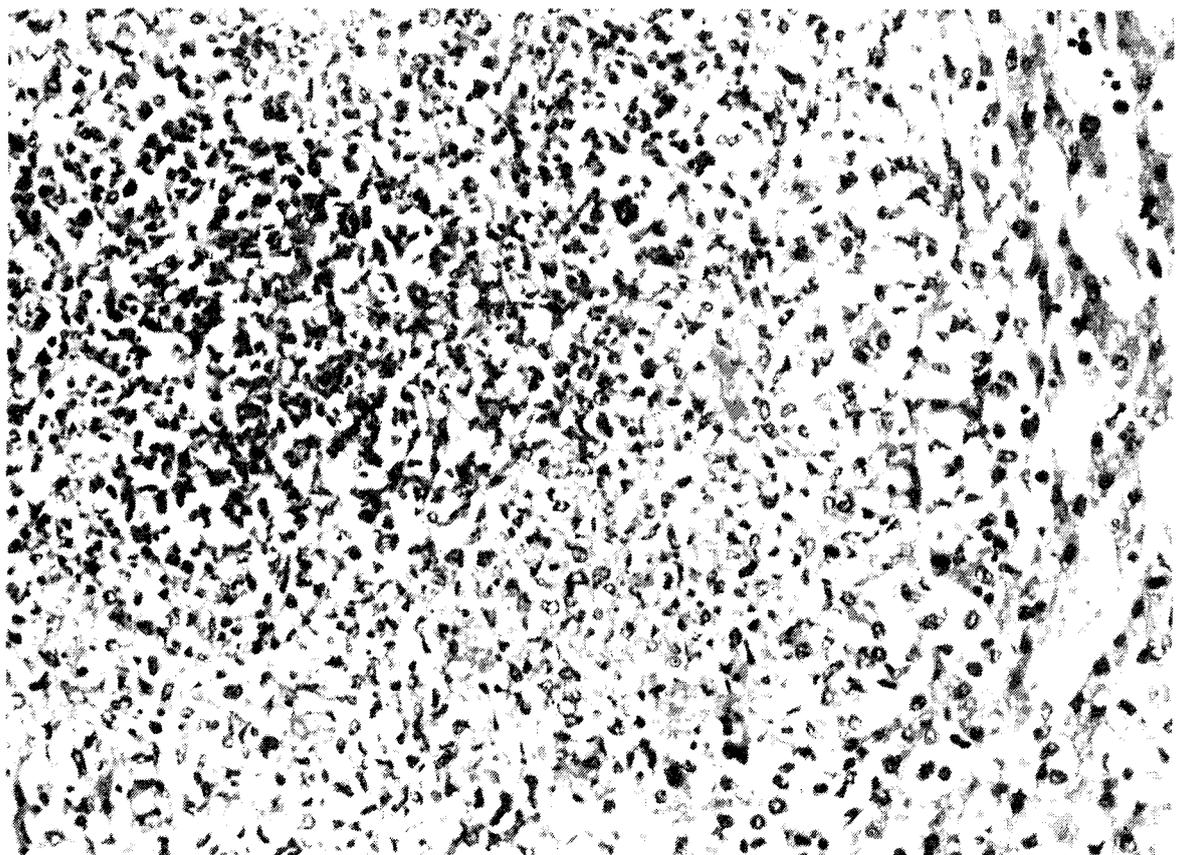


Fig. 7. A well-formed granuloma in the fetal zone of the adrenal, shows epithelioid cell collection around central necrotic area where numerous microorganisms were usually found. H & E \times 350.

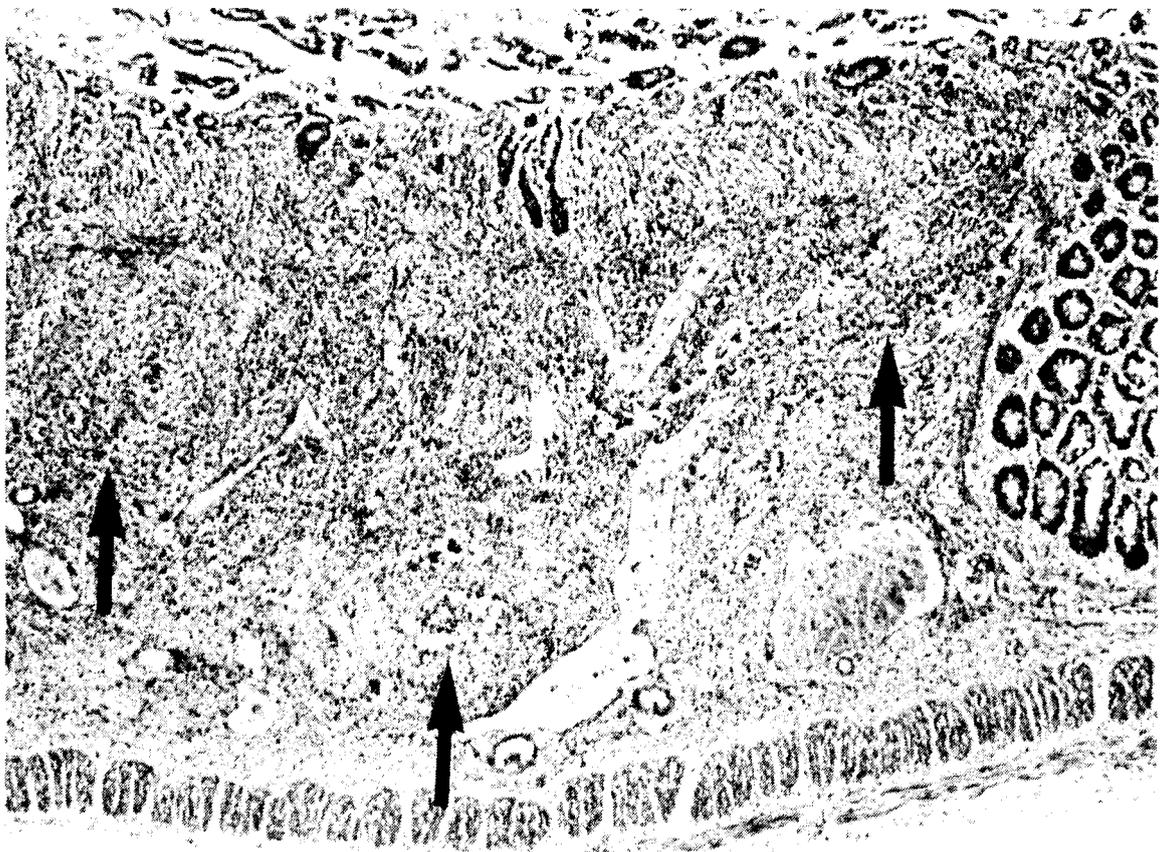


Fig. 8. Ileal mucosa and submucosa show multiple granulomas (arrows) in hyperplastic lymphoid tissue (Peyer's patch). Note the muscle coat is spared. H & E \times 100.

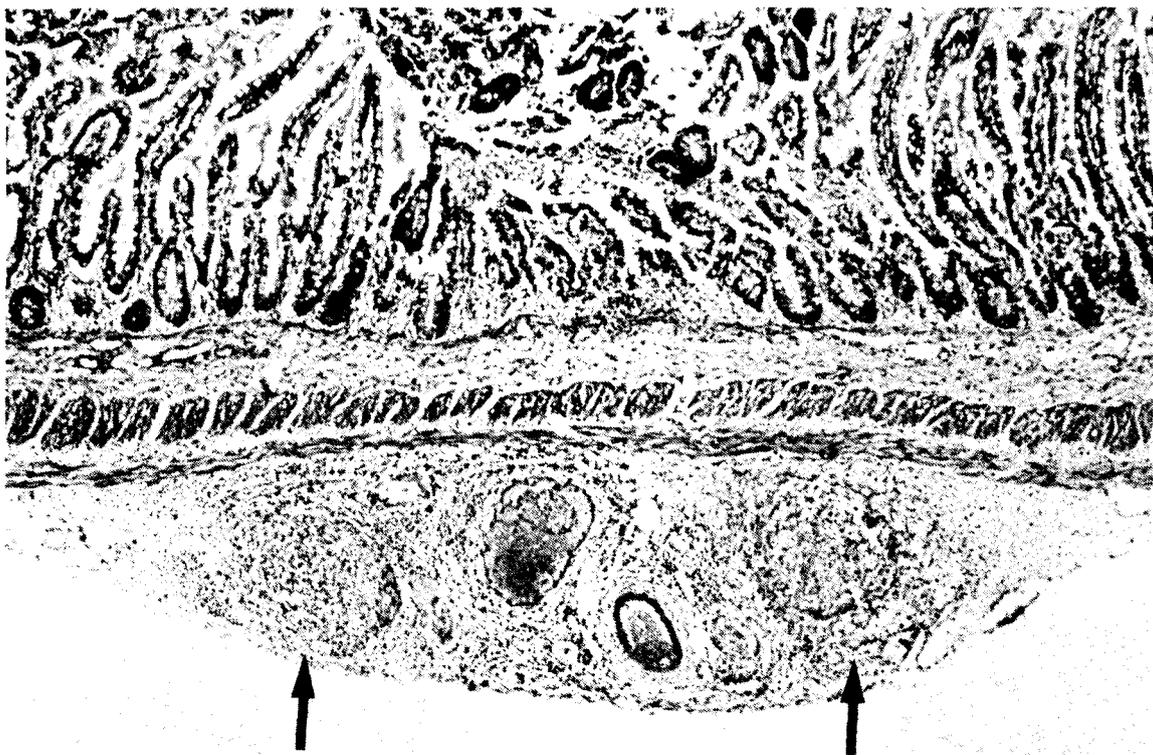


Fig. 9. A focus of serosal granuloma seen in small intestine. Two well-formed granulomas (arrows) and dilated vessels with inflammation are seen. H & E \times 100.

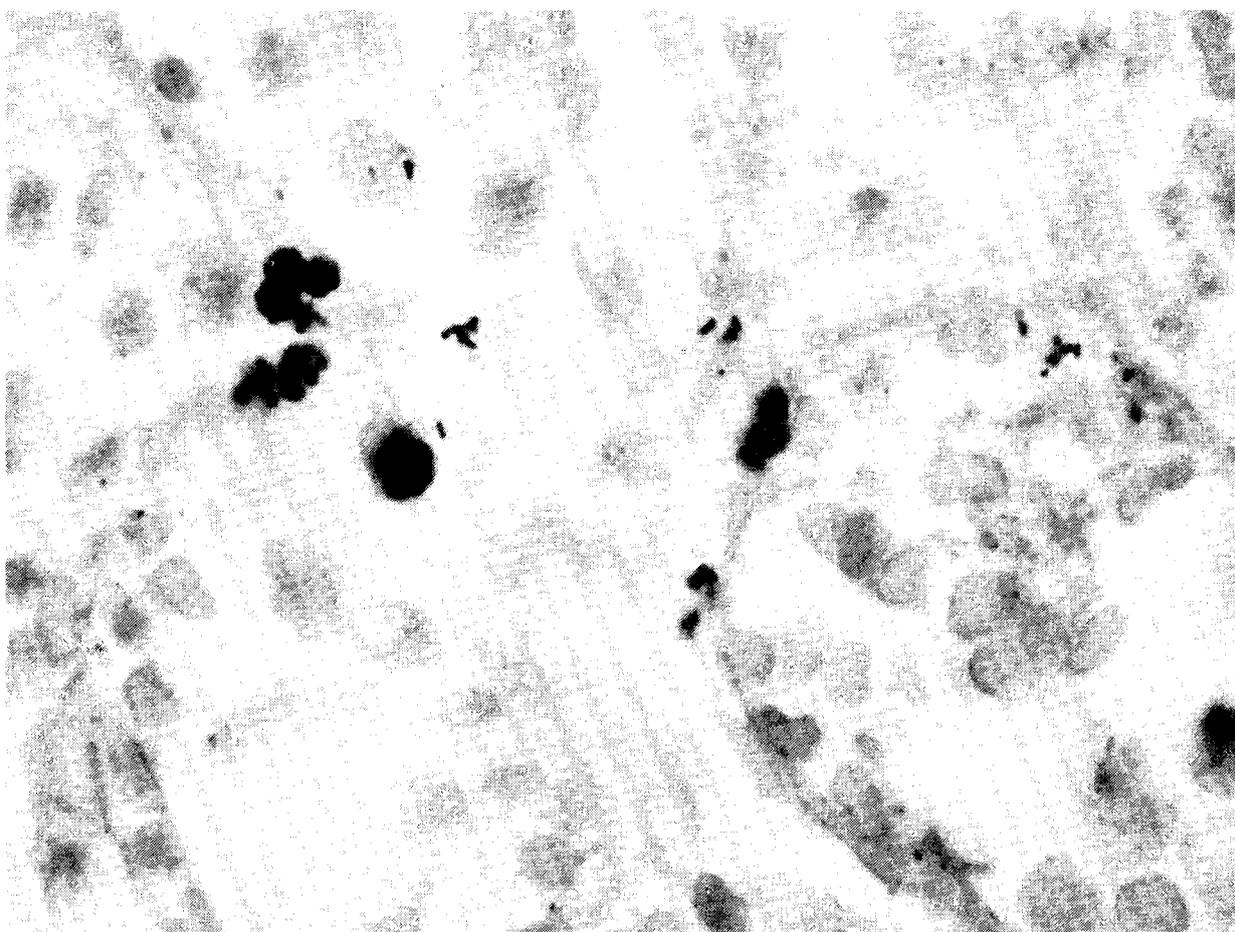


Fig. 10. Bacterial organisms found in the granulomas. They are Gram-positive and stained dark with silver impregnation. Bone marrow, Warthin-Starry stain $\times 1000$.

system was not examined.

Brown-Brenn stain showed numerous cocci in clusters or chains in the tissues involved. They were Gram-positive. These micro-organisms were also positive with Warthin-Starry stains, showing darkly impregnated cocci or rod-like structures (Fig. 10). They were most often seen in the necrotic centers of the lesions. Acid fast stains were negative.

DISCUSSION

Although *Listeria monocytogenes* is widespread in nature and the carrier rate in normal human populations approximate 5 %, perinatal listeriosis is rare (Editorial 1980, 1985). Although most cases are sporadic, outbreaks have been associated with contaminated foods (Schlech *et al*, 1983).

Two groups of patients are commonly affected by listeriosis, the immunocompromized and the pregnant. During pregnancy, characteristically, the women may present with two or more febrile episodes or may be afebrile with an influenza-like illness (Khong *et al*, 1986). There-

fore, the mother of this affected fetus could have passed unnoticed although maternal history is unavailable. Untreated maternal infection invariably results fetal damage in the form of abortion, stillbirth or neonatal sepsis (Relier, 1979).

The confirmation of suspected listeriosis generally requires microbiological diagnosis from culture of blood or body fluids. However, since adult listeriosis is not symptomatologically specific it can be incidentally found to be *Listeria* infection when this organism is cultured from the clinical samples. In Korea there are 6 cases of bacteriologically proven listeria infection (Lee *et al*, 1980). Four of them presented with meningitis and the remaining 2 cases with sepsis. All except one boy were adults with debilitating diseases. The 4 year old child also had malignant lymphoma and presented with meningitis. As far as available literature is concerned there is no case of perinatal listeriosis presented with disseminated granulomatosis in Korea. It is not clear why such cases have never been reported.

It is important to realize for the pathologist that perinatal listeriosis is morphologically diffe-

rent from the adult one. Morphologic diagnosis can be made by the highly characteristic disseminated miliary granulomata, especially when a tissue Gram stain (Brown-Brenn stain in this case) demonstrates short Gram-positive rods in the microabscesses. This is particularly true when we deal with macerated fetuses where the bacteriological study is seldom rewarding. This was true in our case. Although we haven't tried bacteriological culture from the blood, we believe the result would have been unyielding. We like to encourage people to try Warthin-Starry stain if they encounter macerated fetus who show grossly disseminated granulomatous lesion.

It was interesting to note that within the lung the microabscess and granuloma-like lesions were located peribronchially although scattered parenchymal lesions were present. The bronchi showed mucosal necrosis. This together with the presence of vasculitis indicate strongly that

these microbes are angioinvasive thus producing early septicemia and frequent CNS involvement.

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= 국문초록 =

사산아에서 발견된 리스테리아증 (1부검례)

서울대학교 의과대학 병리학교실

지제근

리스테리아 감염은 그렇게 드문것은 아니며 한국에서도 몇몇 임상례의 혈액 및 뇌척수액에서 분리 배양된것으로 보아 임신중 태반을 통하여 태아에 감염되는 이른바 선천성 리스테리아증이 기대되고 있던 중 그린예가 발견되어 이를 보고하였다.

선천성 혹은 주산기성 리스테리아증은 성인례와 달리 전신성 파종성 속립성 및 괴사성 육아종을 나타내어 병리학적으로 대단히 특징적 소견을 가진다. 본예는 33세 임부에서 임신기간 30주만에 사산된 태아로서 부모의 산전 기왕력에 관하여는 전혀 아는 바가 없다. 태아는 나이에 비하여 발육이 불량하였고 부검상 전신 각장기 조직에 파종적 괴사성 육아종을 보였다. 간과비는 커져 있었고 작은 무수한 회백색 결절이 있었다. 그외에도 폐, 식도, 부신, 골수등 많은 부위에 같은 종류의 병변을 가졌고 특히 혈관염을 동반하였다. 중앙에 괴사 및 핵편 그리고 그 주위에 유사괴성 조직구의 증식으로 특징되는 소결절은 그안에 많은 그람 양성균의 구균을 함유하고 있었다.