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# Prenatal Diagnosis of Ascites Caused by Cytomegalovirus Hepatitis

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The case of a 23-weeks-old fetus is described in whom prenatal ultrasonography revealed ascites accompanied by an increased alpha-fetoprotein concentration in the amnial fluid. Detailed embryopathological work-up carried out after induced abortion demonstrated generalized cytomegalovirus disease and furnished histological proof of transplacental propagation.

Epidemiological studies have shown that the ubiquitous cytomegalovirus, a member of the herpesvirus family, is the most frequent causative agent of congenital viral infections in man [14, 15]; about 1% of all neonates are affected. Its incidence varies between 0.5—2.0%, it is more widespread in populations living under primitive conditions [7, 14, 15, 17, 18]. Congenital infection is due to transplacental transmission, the mother is usually a latent carrier [6, 10, 14]. The virus can be transferred by the infected genital secretions during labour or by breastmilk during the postnatal period. In infants and children staying in hospital iatrogenic infection may occur by blood transfusion or organ transplantation [3, 4, 5, 6, 8, 11, 12, 14, 16, 19].

In this paper we report on inclusion body disease due to generalized cytomegalovirus infection developing in utero in a 23-weeks-old fetus in whom subsequent histopathology proved transplacental propagation.

## Report of a Case

C. K. E., a 23 years old woman had visited our genetic counselling clinic during the 21st week of her first pregnancy because her father had had hidden spina bifida, rubella had occurred in her environment during the early stage of this pregnancy and because she had contracted a febrile upper airways infection two weeks earlier. She had a negative family history and had never received blood transfusions. Her serum AFP level was found to be 100 ng/ml, a normal value for 21 weeks according to our norm. Ultrasonography, performed by a Picker LS 2000 device revealed oligohydramnios, thickened placenta and extensive ascites of the fetus (Figs 1 and 2). Eighteen ml amnial fluid was then obtained by transabdominal amniocentesis; its AFP content was much elevated, 34 400 ng/ml (> 2.5 M), cytological examination demonstrated regular epithelial cells and fetal erythrocytes. There was a rubella antibody titre of 1 : 64 and a CMV antibody titre of 1 : 16 in the maternal serum. The couple applied for abortion in view of the ultrasonographic finding and the high AFP content of the amnial fluid. Abortion was induced by extraovular 0.1% Rivanol combined with oxytocin infusion. There were no

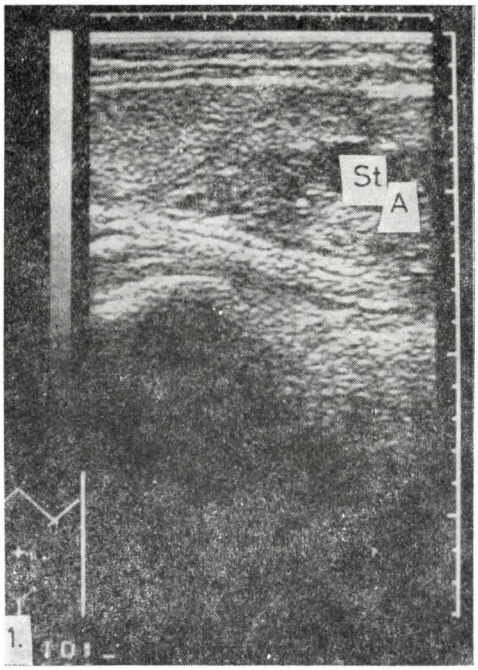



FIG. 1. Ultrasonography. Longitudinal section of fetus revealed ascites distending the abdomen (A), distension of the stomach (st) and conglomeration of the intestines

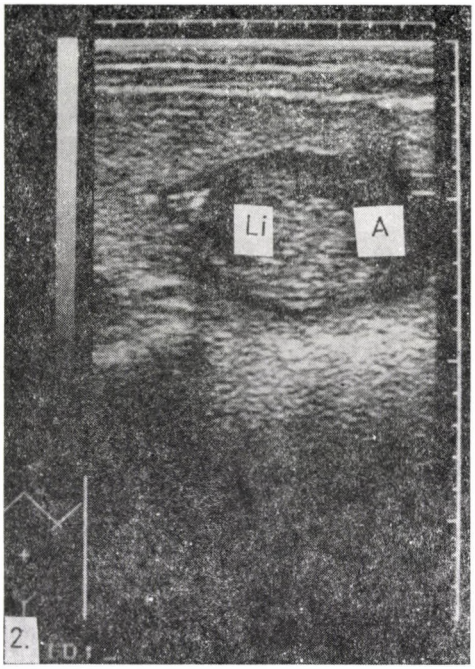



FIG. 2. Ultrasonography. The transversal section at the level of the abdomen demonstrates the presence of ascites (A) between the liver (Li) and the abdominal wall

complications. Detailed pathological examination of the fetus and the placenta was carried out.

There were petechiae on the skin all over the body, the subcutaneous tissue was oedematous and of gelatinous appearance. The abdomen was distended, the abdomen protruded 5 mm above the thoracic level (Fig. 3). A normal intrathoracal situs was seen, diffuse punctuated haemorrhagic foci were found on all serous membranes. The intrathoracic organs showed no abnormality. The abdominal cavity contained 40 ml light-yellow fluid. The abdominal

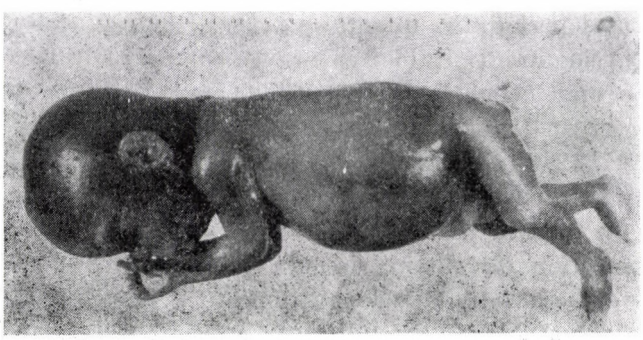
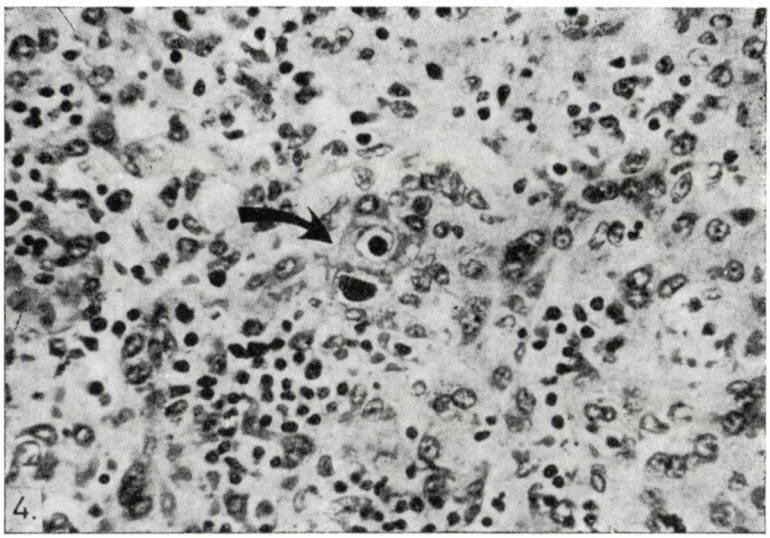


FIG. 3. The aborted fetus shows a striking prominence of the distended abdomen

situs was normal. The hepatic margin exceeded the costal margin by 10 mm, the surface of the liver exhibited diffuse, fine, uniform granulation. No macroscopic changes could be detected in the remaining abdominal and pelvic organs. The shape of the brain was normal, its surface was smooth and exhibited no gyration yet, the cerebral ventricles were of normal width.

Histology showed that the lobular structure of the liver was retained only in



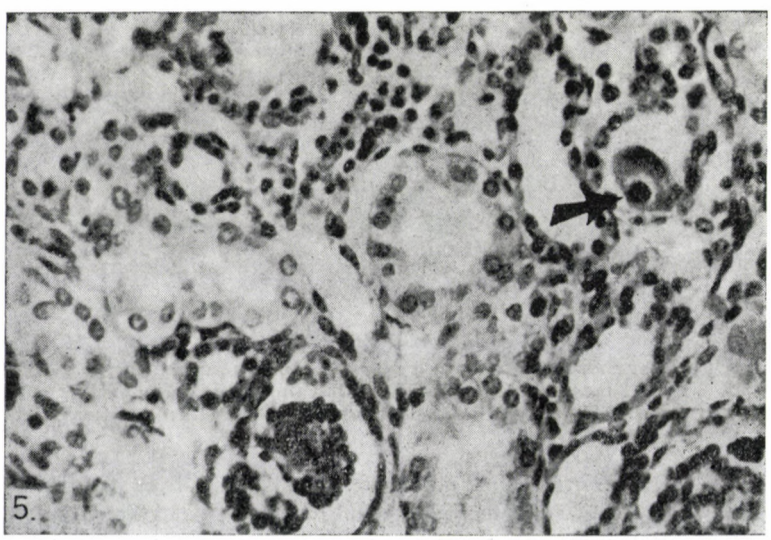




FIG. 4. Irregular pattern of liver cell trabeculae. Nuclear inclusion bodies in the liver cell indicated by arrow, extramedullary haemopoiesis in the sinuses. Haematoxylin-eosin staining, 400-fold magnification

FIG. 5. Inclusion body in an epithelial cell of a renal tubule (arrow). Haematoxylin-eosin staining, 400-fold magnification

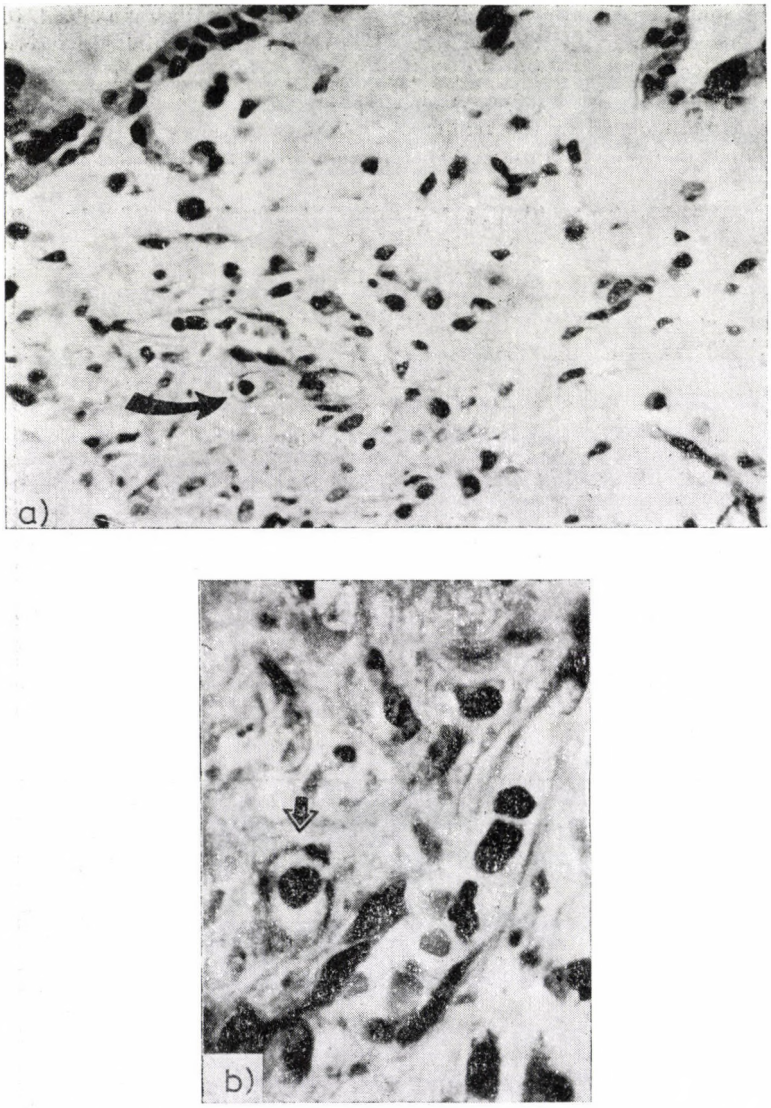



FIG. 6. a) Intranuclear inclusion body in a placental stroma cell (arrow). Haematoxylin-eosin staining, 400-fold magnification. b) The same inclusion body by larger magnification (arrow). Haematoxylin-eosin staining, 1000-fold magnification

small areas, a large proportion of the parenchyma consisted of disintegrated liver cells. Bile duct proliferation, proliferation of collagen fibres, lymphocytic infiltration and connective tissue formation, also propagating between the liver cell trabeculae, were encountered. In some areas ballooning liver cells, focal necrosis and intracytoplasmic retention of bile pigment were observed. Characteristic intranuclear cytomegalovirus inclusion bodies were seen both in epithelial cells of the bile ducts and in the hepatocytes (Fig. 4). Similar intranuclear inclusion bodies were

found in the kidneys, in the mesangium of the glomeruli and in the tubular epithelium (Fig. 5), in the alveolar epithelial cells of the lungs, in the glandular and ductal epithelium of the pancreas and in the stroma cells of the placenta (Fig. 6).

## Discussion

Neonatal cytomegalovirus disease can take two forms: the newborn may suffer a congenital infection due to intrauterine transmission or may contract the infection during the perinatal period [6]. Intrauterine transmission usually takes place during late pregnancy and its source may be either a recently acquired maternal infection or a reactivation of previously contracted, latent maternal infection [9, 14]. The latter form indicates that maternal antibodies do not sufficiently protect the fetus [13]. Infection with the virus usually leads to chronic disease of the fetus, newborn or infant, with alternating exacerbations and periods of latency accompanied by sustained shedding of the virus. In certain cases acute symptoms may develop but the chronic form with late onset is more frequent [15]. The incubation time of the infection acquired during the perinatal period is 4—12 weeks, 8 weeks on the average. Typical symptoms develop in 5% of all congenital infections, another 5% exhibit atypical clinical symptoms and in 90% of all infected cases there is no manifestation during the neonatal period [2, 7]. Clinically typical cases are characterized by multiple organ affection, the reticuloendothelial system and the central nervous system being most involved. Petechiae, hepatomegaly, splenomegaly and jaundice are the most striking features. Since cytomegalovirus infection is the most frequent cause of congenital hepatitis, liver biopsy and its careful histological examination has been recommended in cases affected by hepatosplenomegaly and septic jaundice [1]. Teratogenicity of the virus is a matter of controversy.

Prognosis of infants affected by congenital cytomegalovirus infection is good in the majority of cases but it has been proved that loss of hearing, chorioretinitis, neurological and dental sequelae may develop, manifesting usually during the second year of life [15]. In our case the most severe abnormalities were found in the liver, the pathological finding corresponded to that of red hepatic atrophy. The consequences of the liver changes — hypoproteinaemia due to extensive destruction of hepatic parenchyma and ascites — allowed to arrive at the diagnosis by help of ultrasonography. The detailed histological examination has proved the presence of generalized cytomegalovirus disease and its transplacental propagation.

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