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Cytomegalovirus Infection — Cause of Death at Infancy

D. Radoinova

Department of Forensic Medicine, Medical University, Varna

The purpose of this study is to draw attention on cytomegalovirus infection as one of the most frequent infections among infants and most frequent infection in foetus. Its generalized forms could be the basic factor in thanatogenesis at neonatal and infant age and its localized forms — favourable area for the development of other infections with fatal outcome. We introduce 7 children at the age of up to one year, three of them with generalized form of cytomegalovirus infection and the rest with localized ones. We examine specific morphological changes in the salivary glands and in the affected by the virus organs as well as the rest of the pathomorphological changes.

Key words: Human Cytomegalovirus (HCMV) infection, morphological changes, cause of death.

Introduction

The Human Cytomegalovirus (HCMV), together with the Herpes simplex virus belongs to the Herpesvirudae family, genus Cytomegalovirus. The foetus, newborn babies and infants up to one year are the most sensitive to the virus. It is well known that the HCMV infection is widely spread among pregnant women [1]. The number of children born in Europe and in USA every year with congenital HCMV infection is 40 000 [2]. In Bulgaria the in utero infection is also the most frequent case [5]. This infection in itself could be the cause of abortion or premature birth with heavy damages of various degrees [3]. The proving of the HCMV infection is achieved through IgM-tests (proving an antivirus antibodies in the serum) [5].

The Human Cytomegalovirus destroys the epithelial cells, since it has a definite affinity for gland epithelium, but also organs of different structures could be affected such as nerve and mesenchyme elements [4]. In the damaged cells appear typical intranuclear and cytoplasmatic inclusions usually between the 10^{th}-72^{nd} day after the infection [3]. Around the intranuclear inclusion setts in an area of brightness in the nucleoplasma, wich gives the cell a typical likeness of an "owl's eye".

Clinical manifestation of HCMV infection after birth are numerous: icterus prolongatus and hepatosplenomegalia, transitory thrombocytopenic purpura, hepatitis, encephalitis or other damages of the central nervous system with cerebral calcifications, pneumonia, haemolitic desease etc. [6]. The removal of HCMV from

the human organism is through the urine, saliva, sweat and faeces (when gastroenteral tract is infected).

Morphological changes with HCMV infection are so very specific that no virous confirmation of the diagnosis is necessary. We observe a specific giant-cell metamorphosis (transformation) of contaminated by virus cells (cytomegali) and lymphoid-histiocid infiltration in the stroma. The cytomegali have the same structure and staining properties, independently of their localization in tissues and organs [7, 8, 9].

There are two forms existed of HCMV infection: localized and generalized but this division is relative because under the influence of unfavourable factors the localized form could become generalized [7].

The *purpose* of this study is to accentuate upon the most frequent herpes virus infection especially at neonatal and infant age where it could be the independent cause of sudden death or suitable basis for development of the other infections. We present specific and nonspecific changes in children examined.

Materials and Methods

We present 7 children of age between 4.5 and 11 months, dissected in the Department of Forensic Medicine — MU Varna. Four of the children were boys and three girls. Five children had died in their homes in apparently good health, one of them had been in hospital for cautery and died on 11th day after the accident. The 7th child had been hospitalized for spasmodic bronchitis a week before exitus letalis and had a sudden death without visible symptoms. All children were born in due time with the exception of one first degree prematurely born. Five of the children were Gipsies, one was Bulgarian and one was Turk. Their mothers offered no data about other disease problems during their pregnancy and after birth.

All children underwent histological investigation of internal organs and salivary glands. The materials were stained with by haematoxylin eosin.

Results and Discussion

The external examinations of the children reveal only hypotrophy I-II degree in two of them and no disease changes in five. The internal examination reveals inflammatory changes in the lungs, hepatomegalia (in six children), almost wholly moderately expressed increasing of the lymph nodulae, dystrophic changes in parenchim organs, and thymus atrophy.

The histological investigation showed that in all cases there was cytomegal damage of the salivary glands in the form of giant-cell transformation of the epithelium of the ducts and round-cell infiltration of the part of the stroma, hyperplasia of the lymph foliculi, sometimes (when quantity of the cytomegali is not big) — fibrosis, kystosis and increasing of fat tissue (Fig. 1).

In all children there are established inflammatory changes expressed in various degrees in the lungs and respiratory tract. Five of the children had intersticial pneumonia, the child with cautery was with massive confluencing and abscessing bronchopneumonia, abscessing bronchitis and sepsis and the last of the children was with scattered catarrhal bronchopneumonia and bronchiolitis. Depending on the etiology of the pneumonia the morphological changes in the lungs have some peculiarities in the form of massive haemorage, growing of the bronchial epithelium

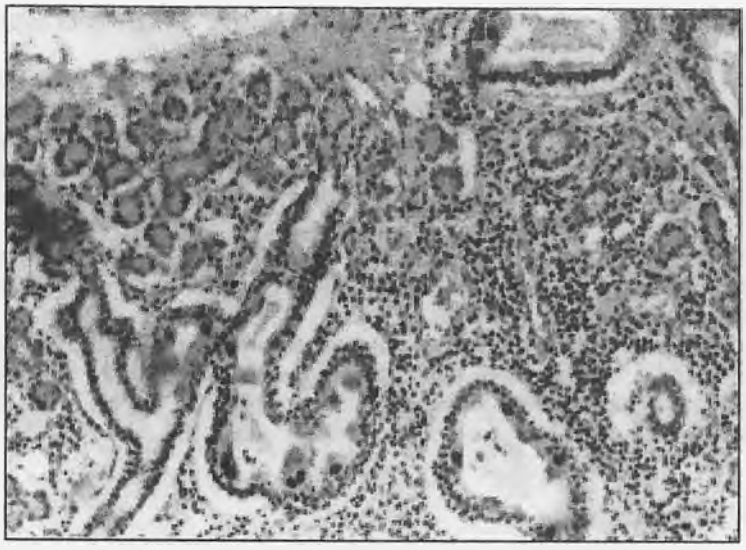

Fig. 1. Salivary gland with cytomegali in channels and infiltration in the stroma (stain HE, × 150)

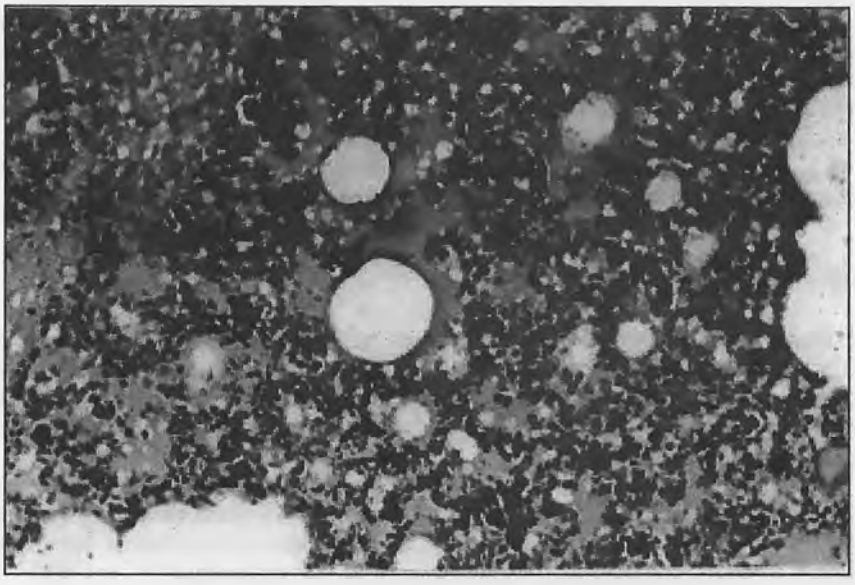

Fig. 2. Lung — dispersed intersticial and intersticial-desquamative pneumonia, irregular airiness, and oedema, cytomegals (stain HE, × 100)

resembling small cushions with paragrippe etc. In all cases there are irregular airiness with dispersed athelectasis, disorder in blood circulation and in some places serosive exudate in the alveoli mixed with scaled cells of the alveolar epithelium and macrofagi and scaling of the bronchial epithelium.

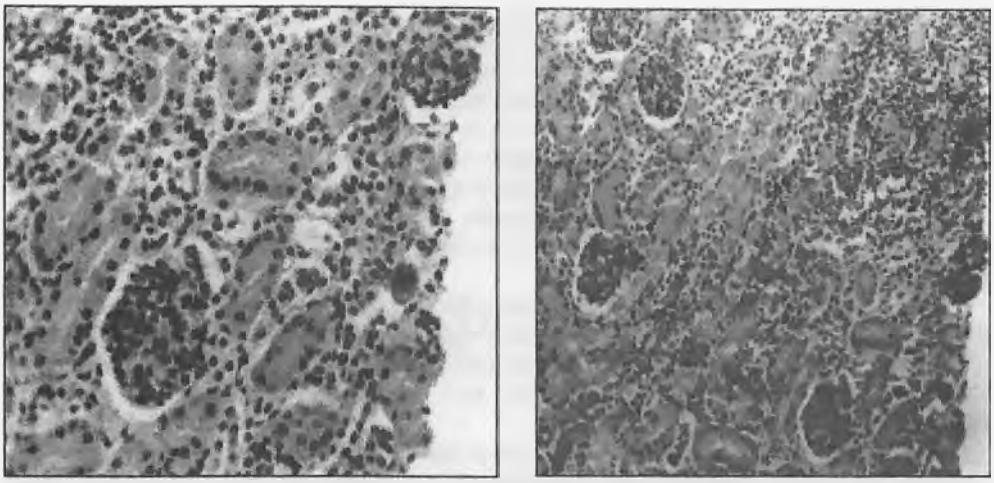

Fig. 3, 4. Kidney with cytomegal transformation cell in the channels (stain HE, × 200) and dispersed cytomegal nephritis (stain HE, × 100)

In three of the seven children there was obseved generalized HCMV infection in the lungs, kidneys, salivary glands and small intestines and in one of them also in the liver. In the lungs was seen cytomegal transformation of the epithelium of the small bronchi and bronchioli, as well as of the bronchial glands. At the same time bronchitis, peribronchitis, intersticial and intersticial-desquamative pneumonia was developed (Fig. 2). Often the cytomegali in the lungs were placed among not big mono-lympho-histocyte infiltrations.

In the kidneys (Fig. 3, 4) giant-cell transformation was observed in the epithelium channels, sometimes around them there was round-cell infiltrations, but it is possible for the damaged organ not to react. In two of the three cases of generalized HCMV infection in the kidneys was established dispersed cytomegal nephritis, dis-

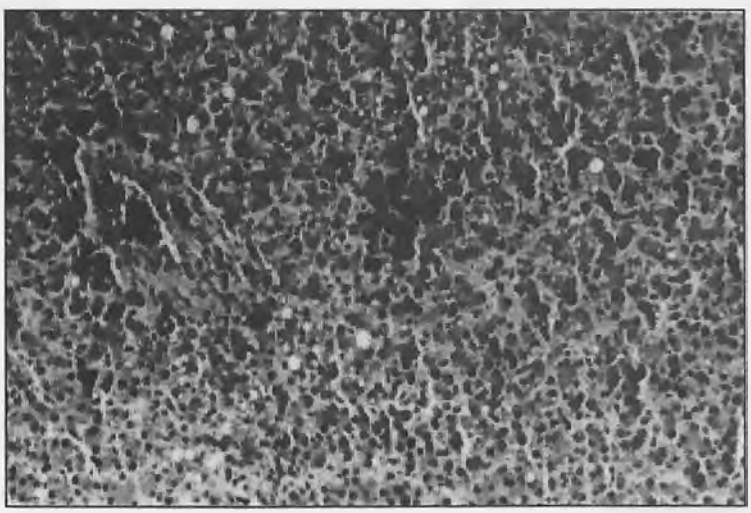

Fig. 5. Liver — parenchim and fat dystrophy with round-cell infiltration

persed membraneous glomerulonephritis with sclerosis of single glomeruls and in the third case we observed focuses with many eosinophiles, epitheloid cells etc.

In the rest of the organs: in all children were observed hyperplasia of the lymph apparatus — lymph nodulae in mesenterium, small and large intestines, peribronchial, perihilar, lymph nodes in the lien. Usually atrophy of the thymus in different degree was established, which means chronic exhausting of the immunity system. Only in one of the children we observed atrophy of the Hassall' bodies with ample increasing the number of lymphocytes. Parallelly to this in all cases there was observed a considerable atrophy of the suprarenal glands (leaf-like, mainly with atrophy of their cortex).

In the other internal organs we had almost always changes of the same type: parenhim and/or fat distrophy of the liver (Fig. 5), sometimes with preserved focuses of extramedular haemopoesis, superficial inflammatory changes in the small and in the large intestines, parenchim distrophy and intersticial oedema of the myocard and cerebral oedema.

Discussing thanatogenesis in the three cases of generalized HCMV infection we take it as a basic disease in the background of which some acute respiratory virus infection might develop and prove to be the direct cause of death. In the remaining four cases we accept HCMV infection to be an accompanying disease, terrain, which strongly favours death because of the general influence of the virosis. One should not forget that the limitation of the HCMV infection is in all cases greater than the limitation of the acute respiratory disease and sometimes is congenital which is proved by the morphological changes in the salivary glands. These opinions disagree with those of N a z a r o v [7], who does not accept the generalized HCMV infection as a basic disease. Contemporary authors [3, 5] agree that this infection is a leading link in the cause of death, in whose background there could also be other ordinary virus infection.

Conclusion

The HCMV infection is diagnosed really easily and should be sought for actively and taken into account in all cases with sudden death especially in infant age. The investigation of the salivary glands gives the quickest direction for detecting HCMV infection in other organs. This diagnosis could lead to specifying the thanatogenesis in any concrete case. On the other hand establishing of HCMV infection is also important for the retrospective searching and proving of a HCMV infection in a mother, respectively a change of behaviour during later pregnancy etc. In a more general sense the exact forensic diagnosis is a part of the fight against numerous complications of congenital HCMV infection.

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